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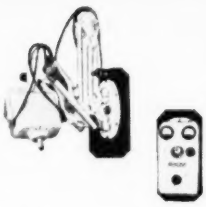

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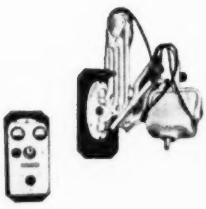

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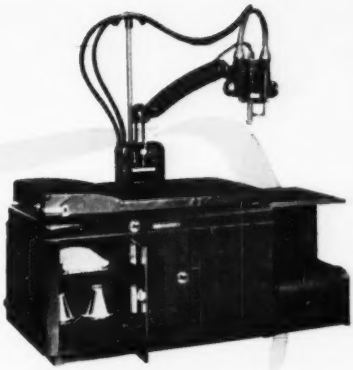

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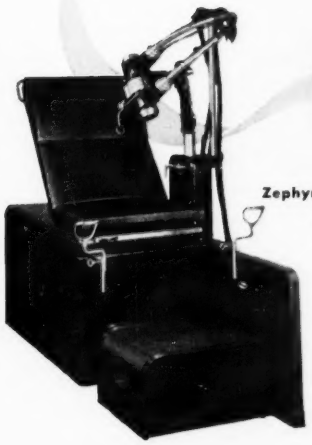

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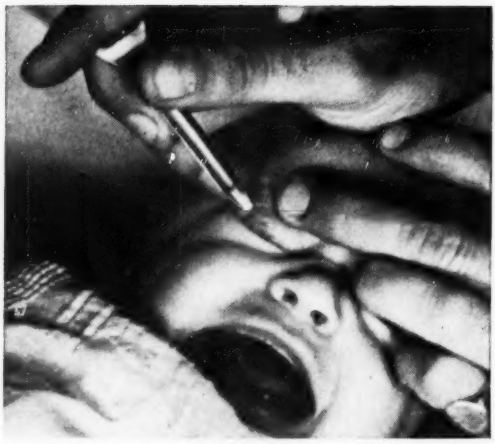
2. Slinger, W. N., and Hubbard, D. M. (1951), *ibid.*, 64:41, July.
3. Sauer, G. C. (1952), J. Missouri M. A., 49:911, November.



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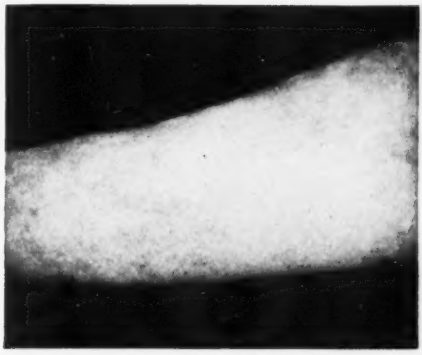

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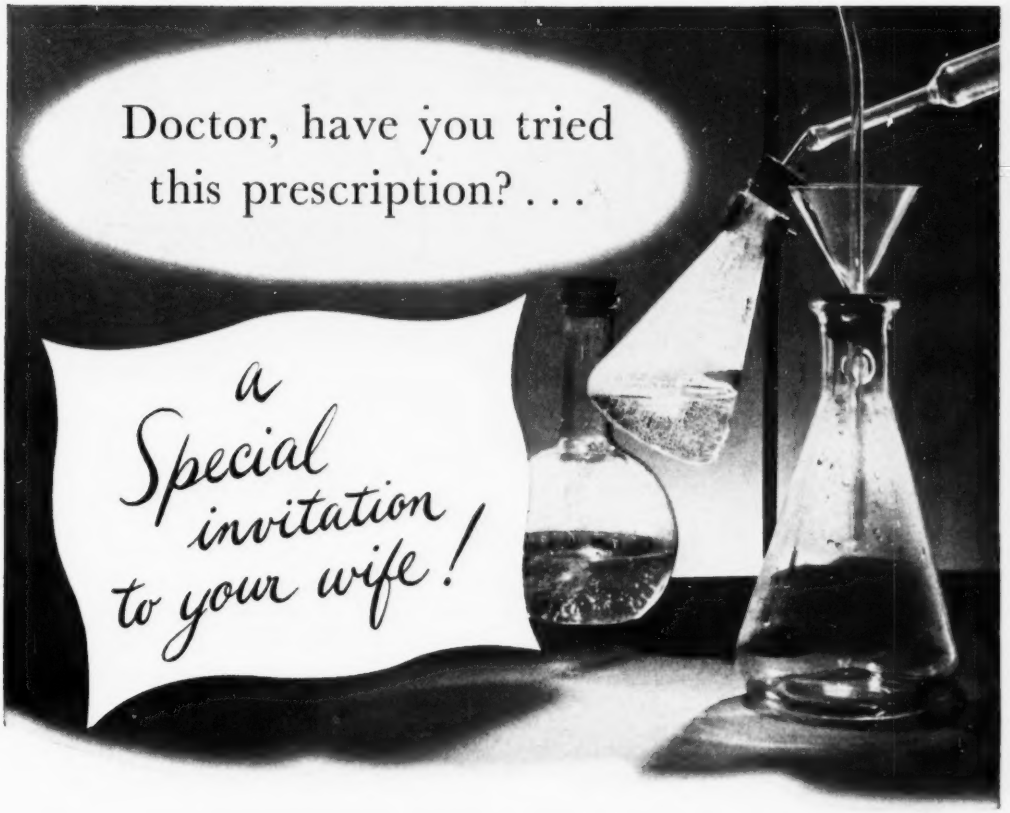

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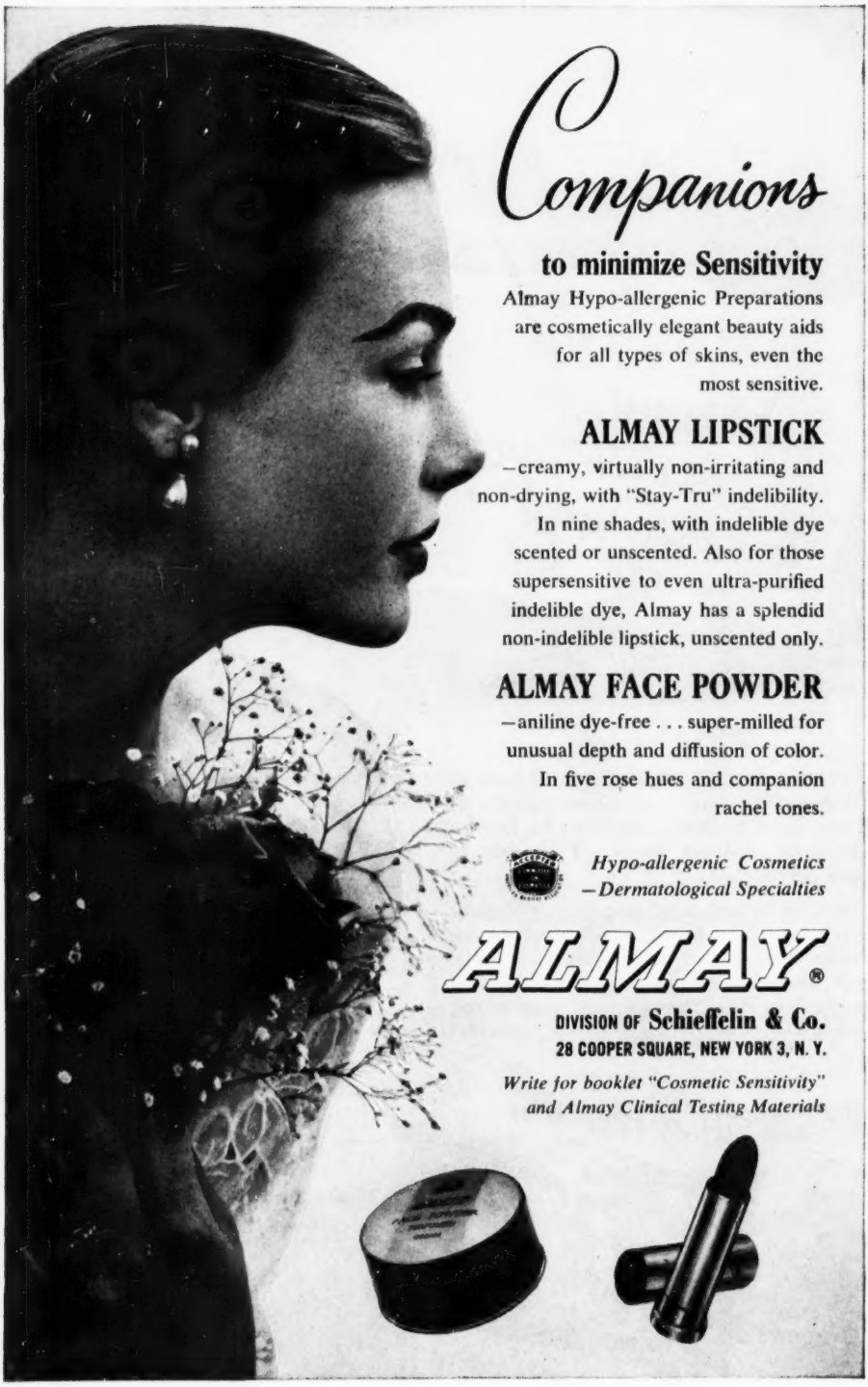

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Archives of Dermatology and Syphilology

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COPYRIGHT, 1953, BY THE AMERICAN MEDICAL ASSOCIATION

RETICULOENDOTHELIAL CELL HYPERPLASIA IN RELATION TO ANTIMONIAL THERAPY OF MYCOSIS FUNGOIDES

JOHN GARB, M.D.
AND
CHARLES F. SIMS, M.D.
NEW YORK

THE PURPOSE of this investigation was to ascertain whether the response of mycosis fungoides to antimonial therapy corresponded to the degree of reticuloendothelial cell hyperplasia found on histologic examination. Eleven cases were studied. The results of the treatment of the first eight patients with antimonials have been reported.[1] The case numbers of the first eight patients in the present report correspond with the order of the case numbers given in the previous publication.[2] Case 9 is omitted because the patient refused further treatment due to pain following a few antimony potassium tartrate (tartar emetic) and stibophen (Fuadin) injections. Case 10 is likewise omitted because a drug eruption developed as a result of the antimony therapy and the treatment was discontinued. Three other cases not recorded in the original publication are herewith added and reported as Cases 9,[3] 10, and 11.

Hematoxylin and eosin stains were used for the histologic study of the cellular infiltrations, and Foot's [4] modification of Bielschowsky's stain was used for the study of the reticulum fibers.

HISTOPATHOLOGIC CHARACTERISTICS

Figure 1 shows a clinically normal skin area from a person without manifest skin or other disturbances.

The reticulum stain reveals very few lattice fibers.

CASE 1 (D. N.; Fig. 2).—A diffuse cellular infiltration in the papillary and subpapillary zones is shown. The infiltration extends upward into the epidermis (exocytosis). The granular

Read before the Tenth International Congress of Dermatology, London, England, July 23, 1952.

From the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School (Dr. Marion B. Sulzberger, Chairman), and the Skin and Cancer Unit of the New York University Hospital.

1. Garb, J.: Antimony Preparations in the Treatment of Mycosis Fungoides, J. Invest. Dermat. **13**:295 (Nov.) 1949.

2. Garb,[1] p. 296.

3. Garb, J., and Fisher, S.: Lymphoblastoma Treated with Antimony Lithium Thiomalate (Anthiomaline), case presented at the Bronx Dermatological Society, New York, April 20, 1950.

4. Mallory, F.: Pathological Technique, Philadelphia, W. B. Saunders Company, 1938, p. 161.

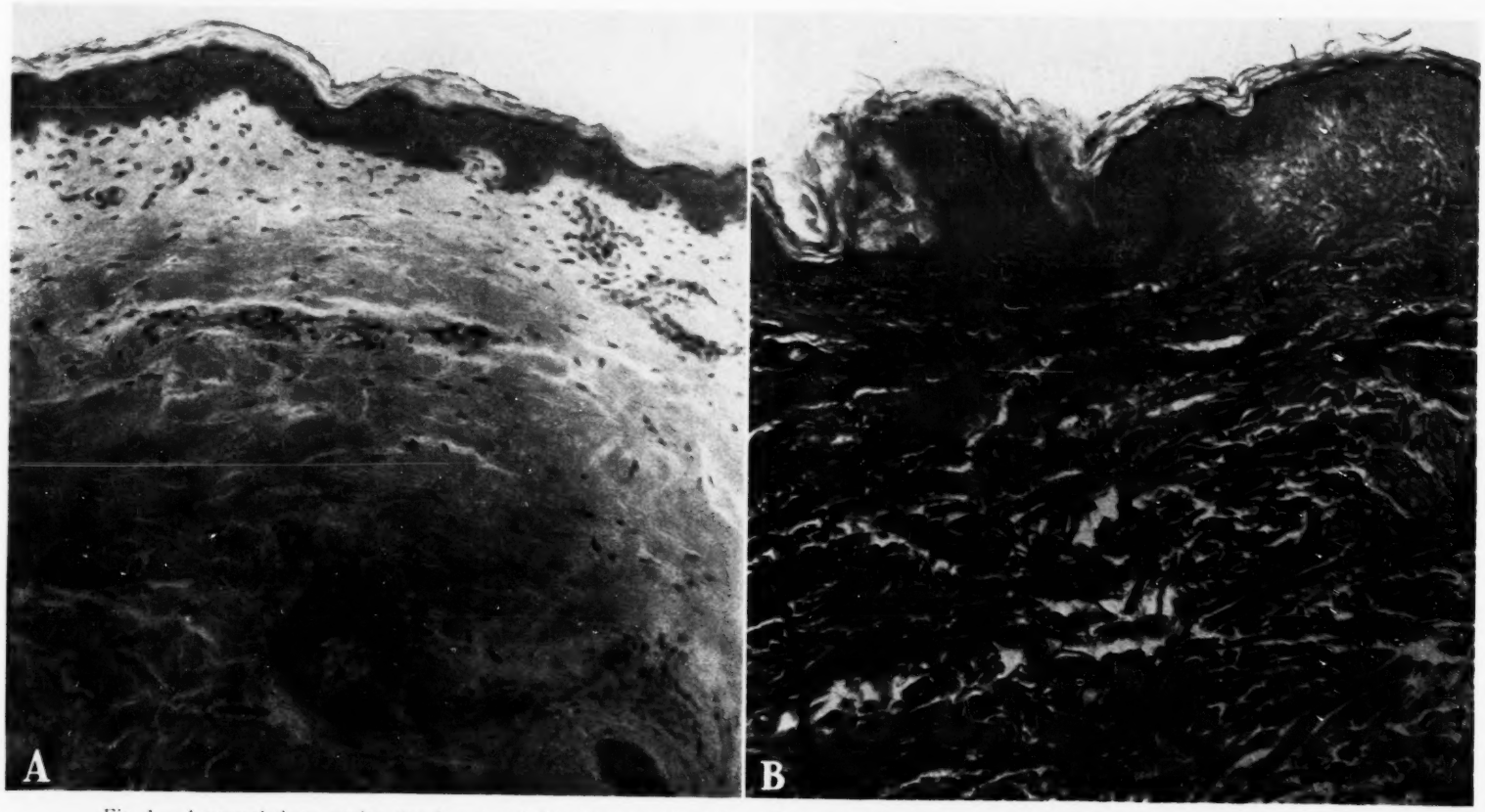

Fig. 1.—*A*, normal tissue section showing normal skin (hematoxylin-eosin). *B*, normal skin showing very few lattice fibers (reticulum stain); × 157.5.

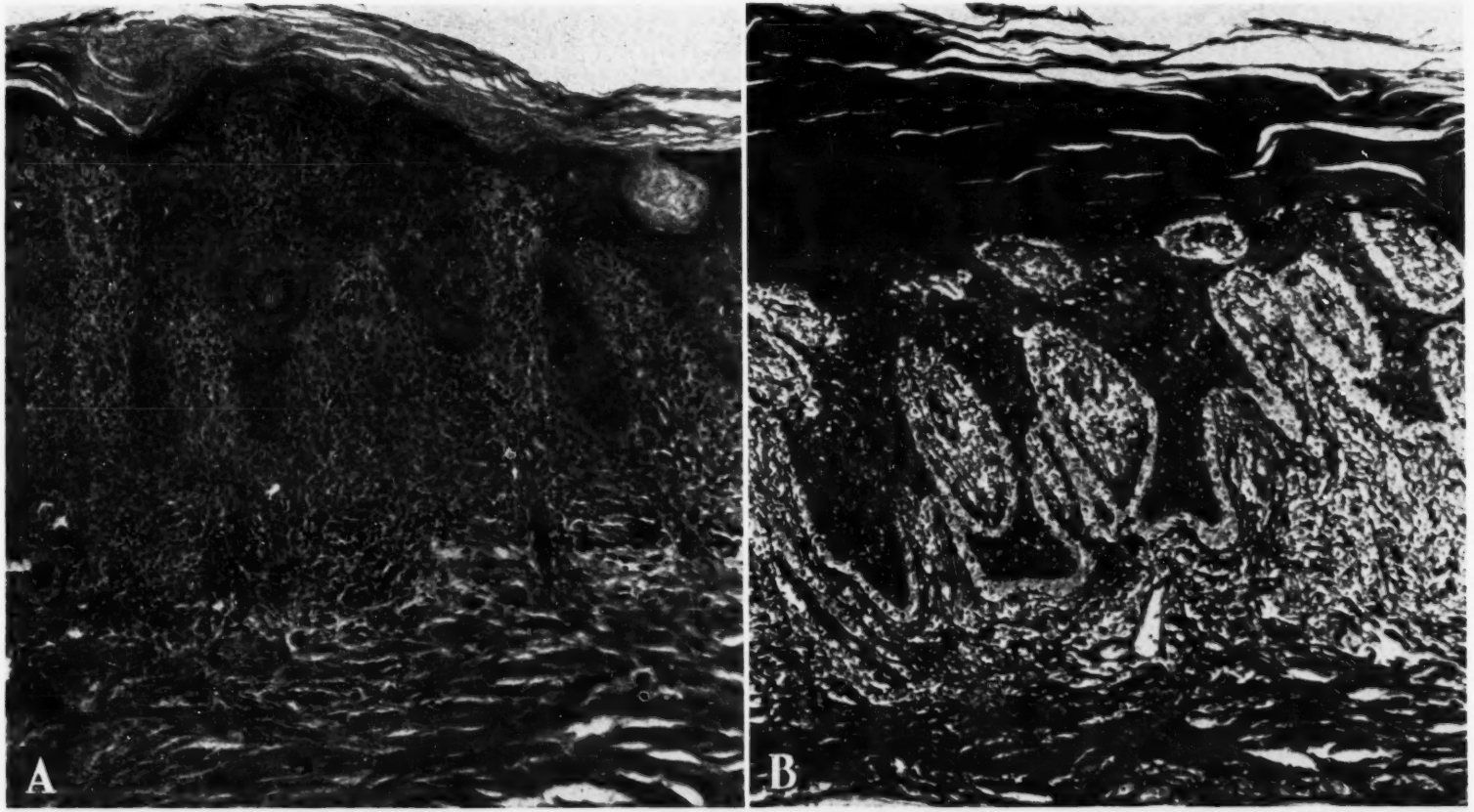

Fig. 2 (Case 1).—*A*, pleomorphic infiltration in the corium. Many large vesicular nuclei resembling so-called mycosis cells are present (hematoxylin-eosin). *B*, showing a very pronounced number of reticulum fibers forming a syncytium throughout the zone of cellular infiltration (reticulum stain); × 157.5.

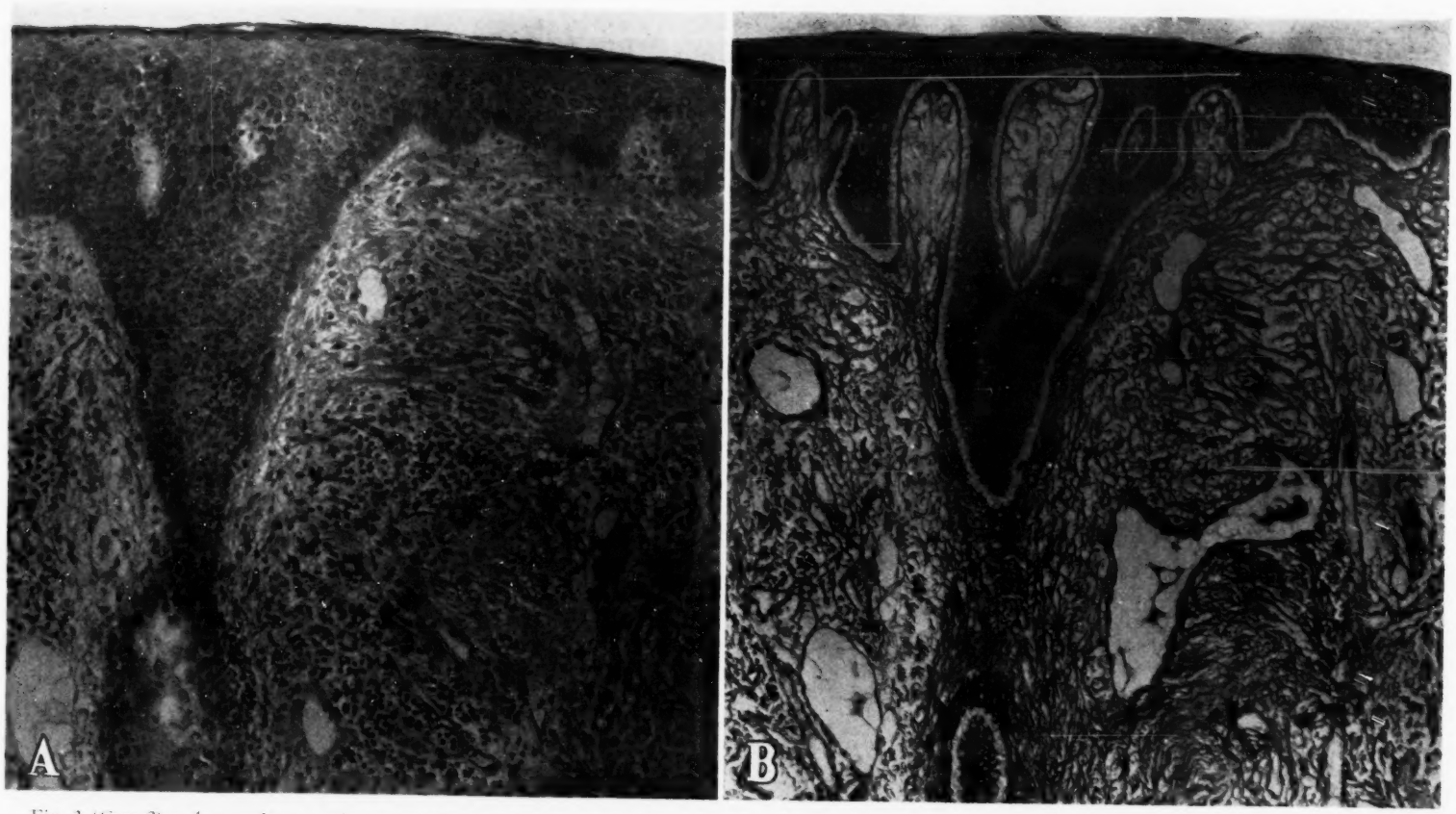

Fig. 3 (Case 2).—*A*, a moderate perivascular cellular infiltration in the upper corium, with some so-called mycosis cells. The reaction is less pronounced than that shown in Case 1 (hematoxylin-eosin). *B*, a moderate number of coarse and fine lattice fibers in the area of cellular infiltration, but much less than in Case 1 (reticulum stain); × 157.5.

layer is absent throughout most of the involved portion of the epidermis. Parakeratosis and a moderate hyperkeratosis are present.

The infiltration in the corium is pleomorphic and presents many small round cells and wandering connective tissue cells. There are also some reticulum, occasional plasma, and polymorphonuclear cells. An occasional mitosis is seen. Many large cells with large vesicular nuclei resembling so-called mycosis cells, but considerably less in number than in Case 4, are present. The vessels of the upper corium are dilated and their walls edematous.

The reticulum stain shows a very pronounced number of fine reticulum fibers, forming a syncytium throughout the zone of cellular infiltration.

CASE 2 (G. F.; Fig. 3).—The epidermis is moderately and irregularly acanthotic. Areas of parakeratosis alternate with areas of retained granular layer. Some exocytosis is noted. In the upper corium there is a perivascular cellular infiltration which consists of a moderate number of small round cells, wandering connective tissue cells, and reticulum cells, with an occasional polymorphonuclear leucocyte. Some large vesicular-type nuclei resembling mycosis cells are scattered throughout the cellular reaction. The perivascular connective tissue framework is loose, edematous, and lacy. The reaction as shown in Figure 3 is less pronounced than that shown in Figure 2.

The reticulum stain reveals a moderate number of coarse and fine lattice fibers in the areas of cellular infiltration, but much less in number than in Case 1.

CASE 3 (V. F.).—A diffuse as well as a perivascular infiltration in the upper corium, not as extensive as in Case 1 but more extensive than in Case 2 is shown. The cellular infiltration is pleomorphic and presents numerous small round cells, wandering connective tissue cells, scattered mycosis cells, and chromatophores. The vessels are dilated, their walls edematous, and their intimal nuclei prominent.

The epidermis is moderately and irregularly acanthotic. The reticulum stain shows a moderate increase in reticulum fibers in the areas of cellular infiltration, similar to that shown in Case 2.

CASE 4 (D. K.).—There is a decided perivascular and diffuse cellular infiltration in the upper corium and in part of the midcorium, approximating that shown in Case 1. The cellular infiltration is pleomorphic and consists of many mycosis cells, small round cells and wandering connective tissue cells, and of occasional plasma cells. The superficial vessels are dilated and their walls edematous. The epidermis is flattened in part.

The reticulum stain reveals a decided increase in reticulum fibers throughout the upper corium and midcorium.

CASE 5 (R. N.; Fig. 4).—The epidermis is mildly irregular, with spotty parakeratosis. There are several Pautrier's abscesses present. A perivascular and diffuse cellular infiltration is seen throughout the upper corium, considerably less than in Case 1, which consists of wandering connective tissue and small round cells, with some plasma and reticulum cells. The vessel walls are edematous and their intimal nuclei prominent. Edema of the collagen is seen in the upper corium.

The reticulum stain shows a small number of fine reticulum fibers in the upper corium about the zone of infiltration, a very poor response.

CASE 6 (R. F.; Fig. 5).—A prominent perivascular and diffuse cellular infiltration in the upper corium and part of the midcorium, similar to Case 1, is shown. The cellular infiltration is pleomorphic and presents small round cells and wandering connective tissue cells, with some mycosis cells. The epidermis is irregularly acanthotic, revealing spotty parakeratosis and occasional Pautrier's abscesses.

The reticulum stain shows a moderate increase in reticulum fibers in the zone of infiltration, similar to that shown in Case 2.

CASE 7 (P. H.).—There is a diffuse perivascular cellular infiltration in the upper corium, nearly as extensive as in Case 1. It consists of many small round cells and wandering connective tissue cells, with some scattered mycosis cells. The epidermis is flattened, showing some areas of spongiosis, probably due to some application of medication.

The reticulum stain reveals an increase in reticulum fibers.

CASE 8 (C. G.).—There is a perivascular and diffuse cellular infiltration, more than that shown in Case 1, in the upper corium and in part of the midcorium. There is a pleomorphic cellular infiltration consisting of many mycosis cells, more than that shown in Case 4, small round,

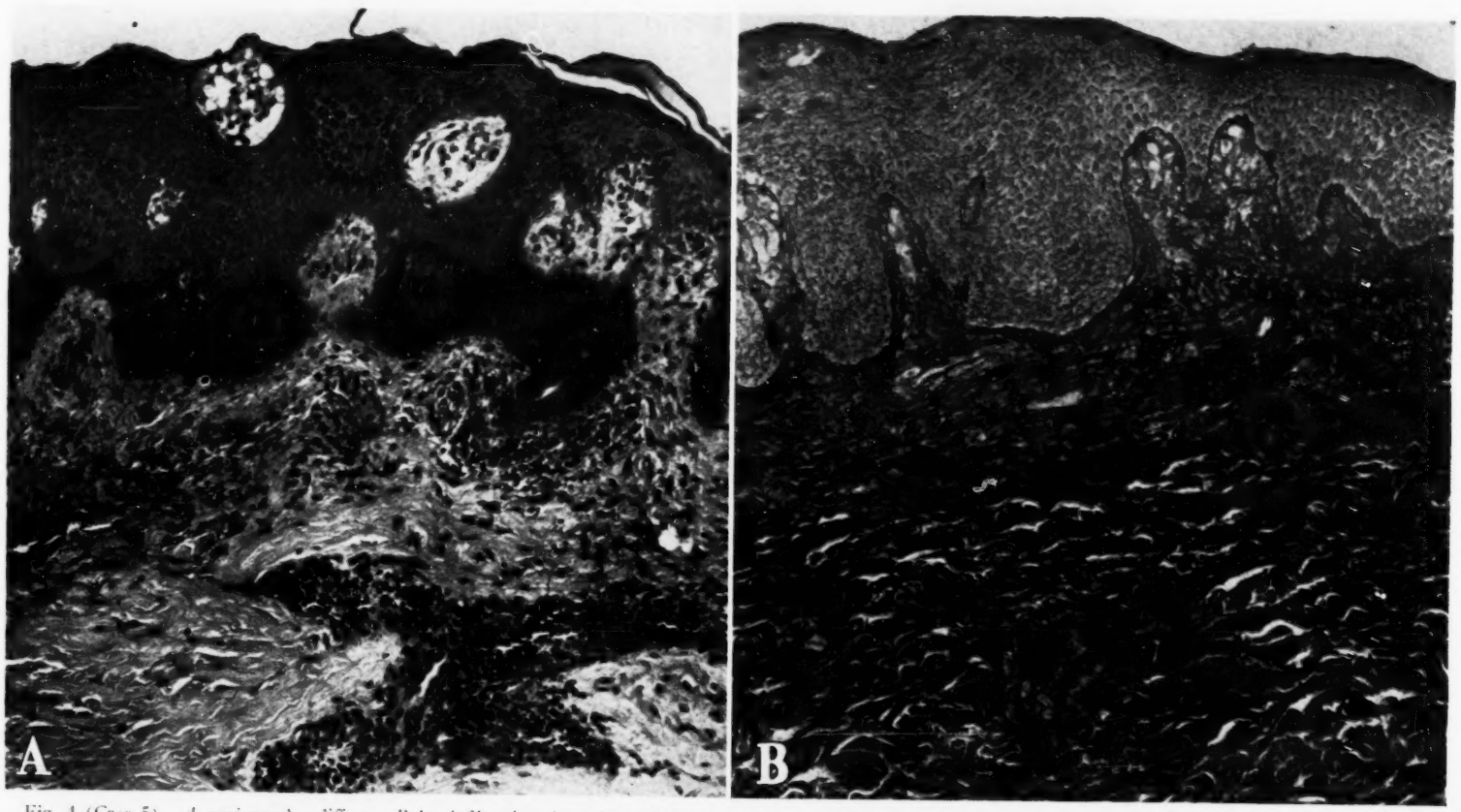

Fig. 4 (Case 5).—*A*, perivascular diffuse cellular infiltration throughout the upper corium, much less than in Case 1. Note Pautrier's abscesses (hematoxylin-eosin). *B*, revealing only a small number of fine reticulum fibers in the upper corium about the zone of infiltration, a very poor response (reticulum stain); × 157.5.

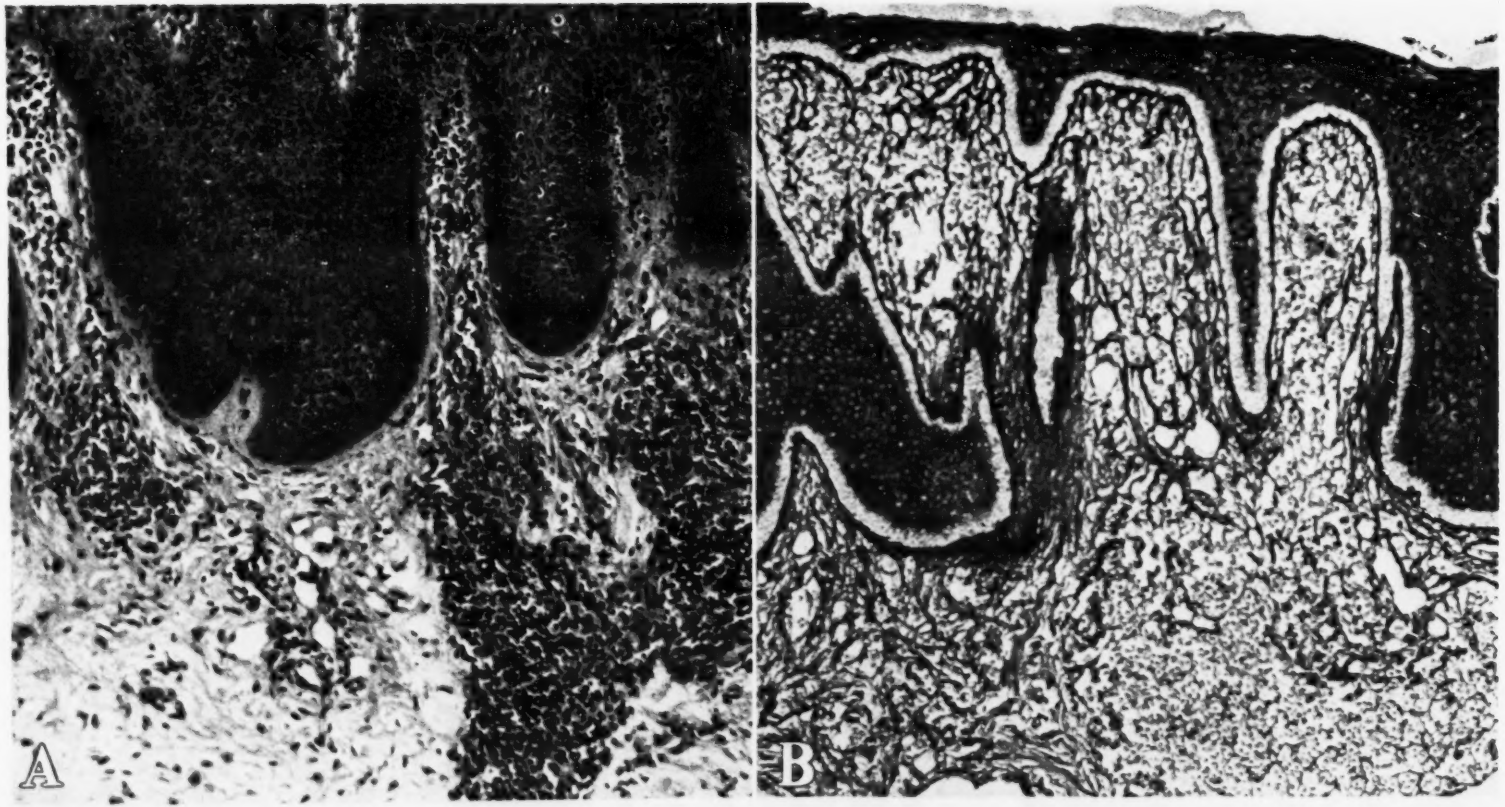

Fig. 5 (Case 6).—*A*, section taken Sept. 18, 1947, showing the pleomorphic cellular infiltration, with some mycosis cells and occasional Pautrier's abscesses (hematoxylin-eosin). *B*, a moderate increase in reticulum fibers in the zone of infiltration, similar to what is shown in Case 2 (reticulum stain); × 157.5.

wandering connective tissue and plasma cells, with occasional eosinophiles. The superficial vessels are dilated. The epidermis is irregularly acanthotic.

The reticulum stain shows a moderate increase in reticulum fibers in the upper corium.

CASE 9 (W. F.).—There is a diffuse cellular infiltration in the papillary and subpapillary zones, similar to that shown in Case 1. The infiltration is pleomorphic in character and consists of small round cells, histiocytes and wandering connective tissue cells, with an occasional eosinophile. There are a few scattered mycosis cells and mitotic figures. The epidermis is irregularly acanthotic, presenting focal and spotty parakeratosis.

The reticulum stain shows a moderate increase in the reticulum fibers.

CASE 10 (H. V.).—There is a diffuse cellular infiltration in the upper corium, which is pleomorphic and which consists of many reticulum cells, some round cells, wandering connective tissue cells, occasional chromatophores, and fibroblasts. There is pronounced edema in the area of infiltration. The epidermis is mildly and irregularly acanthotic and presents many Pautrier's abscesses.

There is a decided increase in reticulum fibers in the area of infiltration.

CASE 11 (M. B.).—There is a rather extensive perivascular cellular infiltration extending from the upper to the midcorium. The infiltration is pleomorphic and consists of many reticulum cells, some small round cells, wandering connective tissue cells, and fibroblasts. The connective tissue framework is considerably altered in the area of infiltration. (It is rarified, and in many areas the fibers are absent.)

The epidermis is irregularly acanthotic, presenting areas of spongiosis and vesicle formations, as well as spotty parakeratosis. The vessels are dilated throughout and their walls edematous.

The reticulum stain reveals a decided increase in the number of reticulum fibers in the area of infiltration.

RETICULOENDOTHELIAL SYSTEM

For a better understanding of this paper it was thought advisable to give a review of some of the prevailing concepts regarding the reticuloendothelial system and the histologic features of mycosis fungoides. The name of reticuloendothelial system was given by Aschoff [5] to two groups of cells widely distributed throughout the body, namely, the endothelial cells and the irregular elongated cells known as reticulum cells. These cells appear to be undifferentiated or partly differentiated mesenchymal depots which persist in postnatal life and are, under suitable circumstances, capable of further elaboration.[5a]

Comprising a part of this system are the fixed endothelial cells lining the blood sinuses of the spleen and the sinuses of the lymph nodes, the capillaries of the bone marrow, the adrenal cortex, the pituitary, and the liver (stellate cells of Kupffer). Forming also a part of this system, all of which are more or less identical and probably derived from the endothelium, are the wandering cells of tissues, variously known as histiocytes, endotheliocytes, clasmatocytes, spleenocytes, and macrophages. Cells of the adrenal glands and the heart (myocytes) have recently been shown to possess phagocytic properties, and their relationship to the reticuloendothelial system is under discussion. The microglia cells of the supporting structure of the brain are of mesodermal origin and are also phagocytic cells. They should be included in the reticuloendothelial system.[6]

5. Aschoff, L.: Das reticulo-endotheliale System, Ergebn. inn. Med. Kinderh. **26**:1, 1924; cited by Jaffee, R. H., in Downey, H., Editor: Handbook of Hematology, New York, Paul B. Hoeber, Inc., 1938, Vol. 2, p. 979.

5 (*a*). Wintrobe, M. M.: The Reticuloendothelial System, in Tice, F.: Practice of Medicine, Hagerstown, Md., W. F. Prior Company, Inc., 1940, Vol. 6, p. 720.

6. Bailey, F. R.: Bailey's Text-Book of Histology, revised by P. E. Smith and W. M. Copenhaver, Ed. 12, Baltimore, Williams & Wilkins Company, 1948, p. 269. Richter, M. N.: The Reticuloendothelial System, in Pathology, edited by W. A. D. Anderson, St. Louis, C. V. Mosby Company, 1948, p. 1010.

The cells of the reticuloendothelial system possess certain similarities in morphology and function. Their best-known function is phagocytosis and storing of foreign particles. This may be demonstrated by the injection in the blood stream of vital dyes such as India ink, pyrrole blue, lithium-carmine, or trypan blue. The reticuloendothelial cells become loaded with these particles, while other cells of the body take up only a few granules, if any. The vital or supravital staining reaction is simply a process of ultramicroscopic phagocytosis. The fine particles of the dye are not visible in ordinary cells, because too few granules are taken up to reveal the stain. However, these particles of the vital dyes are more avidly taken up from the injected solution by the cytoplasm of the reticuloendothelial cells, where they accumulate into larger masses. The reticuloendothelial cells then become visible under the microscope and may easily be detected among the ordinary tissue cells, from which it is otherwise difficult to distinguish them.[7] These reticuloendothelial cells, because of their phagocytic properties, have been named macrophages by Metchnikoff,[8] to distinguish them from the smaller neutrophiles or microphages. This property of phagocytosis has been employed as a test of the functional activity of the reticuloendothelial system.

Many of the cells of the reticuloendothelial system, besides their phagocytic traits, also have the function of forming antibodies such as antitoxins, hemolysins, and agglutinins. They have the ability to become cells of the circulating fluid after a process of differentiation, and they become fibroblasts when their defense role is finished.[9] The defense system in the cutaneous structure is represented by the Langerhans cells and by the endothelium of the papillary blood and lymph capillaries.[10]

HISTOLOGIC STRUCTURE OF MYCOSIS FUNGOIDES

Mycosis fungoides presents in the plaque stage typical and diagnostic histologic features. The infiltration varies in density and may or may not be limited to the upper portion of the cutis. It is characterized by multiplicity of cell types, which include lymphocytes, polymorphonuclear leucocytes, histiocytes (mature reticular cells), reticulum cells (immature reticular cells), connective tissue cells of different types, plasma cells, monocytes, and sometimes eosinophiles and mast cells. The so-called mycosis cells, which are immature and atypical reticulum cells, are also present. They differ from histiocytes by their deeper staining and by their nuclei being more irregularly shaped. The nuclei of the histiocytes vary greatly in size and shape and may show clumping to form pseudogiant cells, pyknosis (shrinking) and karyorrhexis (breaking-up). Mitotic figures are usually present.[11]

The epidermis presents varying degrees of acanthosis. Occasionally, Pautrier's microabscesses are seen in the epidermis, which consist mainly of accumulation

7. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice: A Text in Applied Physiology, Baltimore, Williams & Wilkins Company, 1950, p. 104.

8. Metchnikoff, E., cited by Best and Taylor.[7]

9. Best and Taylor,[7] p. 105.

10. Urbach, E., and Gottlieb, P. M.: Allergy, New York, Grune & Stratton, Inc., 1943, p. 796; cited by Garb,[1] p. 305.

11. (*a*) Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, Ed. 7, Philadelphia, Lea & Febiger, 1948, p. 875. (*b*) Lever, W. F.: Histopathology of the Skin, Philadelphia, J. B. Lippincott Company, 1949, p. 426.

of lymphocytes and histiocytes in contradistinction to the microabscesses seen in psoriasis, which consist of polymorphonuclear leucocytes. In the tumor stage of mycosis fungoides the infiltration, as a rule, still shows the same characteristics as in the plaque stage, except that it frequently becomes more uniform in character. There is an increase in the number of mycosis cells and mitotic figures. The histologic picture in this stage often merges with that of reticulum-cell sarcoma. In some cases there may be an increase in reticular or monocytic cells, with longitudinal grooving of the cells, showing a transition to monocytic leukemia of Schilling.[12] In other cases, if the infiltration has many mycosis cells of considerable size which may contain more than one nucleus (thus resembling mononucleated or multinucleated Sternberg-Reed giant cells) the histologic picture may simulate Hodgkin's disease.[13] In this connection it is noteworthy that Fraser and Schwartz[14] reported a case of a 36-year-old woman with necropsy findings of reticuloendothelial disease showing features of mycosis fungoides, Hodgkin's disease, and reticular cell lymphosarcoma.

RETICULUM FIBERS

The reticulum fibers are now generally considered to be "precollagen," or immature collagen, occurring as fine separate fibrils of collagen, which is simply compacted reticulum.[15] Both collagen and reticulum react similarly to all common histologic stains, except to silver impregnation stains. The reticulum fibrils, because of their fineness, are easily penetrated by the colloidal silver, and this probably explains their argyrophilic properties.[16]

Reticulum fibers are most likely formed by mesodermal cells, which secrete an extracellular gelatinizing substance.[17] Various types of mesodermal cells, namely, reticulum cells, histiocytes, vascular endothelial cells, lymphocytes, fat cells, and smooth and striated muscle cells have the ability to form reticulum fibers.

Normal skin contains only a few reticulum fibers, since all the reticulum is present as collagen. A few reticulum fibers are usually seen around arterioles, around glandular parts of sweat glands, and as short thick reticulum fibers in palisade arrangement for defense immediately beneath the basal layer of the epidermis. These fibers contribute to the firm coherence of the epidermis and corium by their extension between the cytoplasmic filaments of the basal cell.[18] In pathologic conditions, however, in which there is a formation of young mesodermal cells, the skin contains numerous reticulum fibers. They are particularly abundant, therefore, in granulomas such as syphilis, tuberculosis, and sarcoid, and

12. Ormsby and Montgomery,[11] p. 875.

13. Fraser, J. F., and Schwartz, H. J.: Neoplastic Disease of the Reticulo-Endothelial System, Arch. Dermat. & Syph. **33**:1, and 5 (Jan.) 1936.

14. Fraser and Schwartz,[13] p. 1.

15. Mallory, F. B., and Parker, F., Jr.: Reticulum, Am. J. Path. **3**:515 (Sept.) 1927; cited by Lever,[11b] p. 17.

16. Nageotte, J., and Guyon, L.: Reticulin, Am. J. Path. **6**:631 (Nov.) 1930.

17. Foot, N. C., and Day, H. A.: The Occurrence of Reticulum in Tumors, Am. J. Path. **1**:431 (July) 1925; correction **1**:681 (Nov.) 1925; cited by Lever,[11b] p. 17.

18. Szodoray, L.: The Structure of the Junction of the Epidermis and the Corium, Arch. Dermat. & Syph. **23**:920 (May) 1931.

in mesodermal tumors such as sarcomas, lymphomas, and histiocytomas. If the mesodermal cells are very immature, as in stem cell lymphoma, they may not possess the ability to form reticulum. If, however, the mesodermal cells are very mature, as in some fibromas, all newly formed reticulum may have become condensed to collagen.[19]

HISTOGENESIS

The late J. Frank Fraser [20] of our school gave a logical interpretation of the different histologic structures in the various stages of mycosis fungoides. In the premycotic state there are a few tumor cells "which struggle for their existence" against the strong defensive inflammatory reaction on the part of the tissue involved. As the disease advances the tumor cells increase, and the inflammatory reaction slows down. Finally, the tumor cells overcome the defense reaction and proliferate uninhibitedly. In the *d'emblée* type of mycosis fungoides there is usually little or no inflammatory reaction, and the tumor features predominate throughout the entire course of the disease.

COMMENT

Mycosis fungoides is recognized as being a disease of the reticuloendothelium of the skin. Fraser [21] states that the cells making up a mycosis fungoides tumor are derived from the adventitial cells of the small blood vessels of the skin. They have been considered as genetically related to the adventitial and periadventitial histiocytes. A number of French authors also favor the view that mycosis fungoides is a disorder of the reticuloendothelium. By using the May-Grünwald-Giemsa staining technique Cottini [22] was able to demonstrate the reticulohistiocytic cells in the imprints of skin tumors and lymph nodes in three cases of mycosis fungoides. He therefore considered mycosis fungoides a disease of the reticuloendothelial system. Berman [23] states that "Cottini's photographs of his imprinted material are more convincing than the evidence which has hitherto been indicated in sections." Berman [24] supports Cottini's opinion that the unknown causal factor acts electively on the reticuloendothelial system, which is capable of provoking the diffuse and generalized picture of the systemic form, as well as the localized manifestations of mycosis fungoides. Berger [25] calls mycosis fungoides a reticuloendotheliosis of the skin. He believes that fibrocytes may undergo a similar transformation as local histiocytes, from which the majority of the mycosis cells develop. Cawley and his co-workers [26] state that the pathological findings in 10 cases of mycosis fungoides

19. Lever,[11b] p. 17.

20. Fraser, J. F.: The Interpretation of Mycosis Fungoides as a Variety of Lymphosarcoma, Arch. Dermat. & Syph. **11**:445 (April) 1925.

21. Fraser,[13] p. 11.

22. Cottini, J. B.: Aspects hématologiques et histopathologiques de trois cas de mycosis fongoide, Ann. dermat. et syph. **8**:15 (Jan.) 1937.

23. Berman, L.: Pathologic Nature of Mycosis Fungoides, Arch. Path. **29**:530 (April) 1940.

24. Berman,[23] p. 540.

25. Berger, L., and Vallée, A.: Le mycosis fungoïde: Une réticuloendothéliose de la peau, Presse méd. **38**:177 (Feb. 5) 1930; cited by Jaffee,[5] p. 1105.

26. Cawley, E. P.; Curtis, A. C., and Leach, J. E.: Is Mycosis Fungoides a Reticuloendothelial Neoplastic Entity? A. M. A. Arch. Dermat. & Syph. **64**:255 (Sept.) 1951.

clearly indicate the alleged reticuloendothelial origin of mycosis fungoides. Herzberg and Ueberschär [27] in a report on five patients interpret mycosis fungoides as a neoplastic disease of the widespread reticuloendothelial system.

EVALUATION OF THE RESULTS OF THE HISTOPATHOLOGIC AND RETICULUM-FIBER STUDIES OF THE 11 CASES IN WHICH THERE WAS TREATMENT WITH ANTIMONIALS

An accurate evaluation of the results could not be made for the following reasons:

1. Only qualitative studies of the cellular infiltrations and the reticulum fibers could be made.

2. These 11 patients comprise a mixed group in various stages of the disease process. It has been the experience of one of us (J. G.)[28] that patients in the tumor and ulcerative stage of long duration, as in Case 1,[29] were often inclined to respond better to antimony treatments than those in the plaque and tumor stage of short duration. A more uniform group, therefore, similar to the group represented in Case 1, would be a better index of the effectiveness of antimonials in mycosis fungoides.

3. It has been the experience and impression of one of us (J. G.)[30] that antimony potassium tartrate is the drug of choice of the antimonials used thus far. However, the case of Berkovsky [31] in which there was treatment with ethylstibamine (Neostibosan) and the case of Fisher,[3] Case 9, in which there was treatment with antimony lithium thiomalate (Anthiomaline) indicate that other antimonials may be be effective or even more effective than antimony potassium tartrate. Only in Cases 1, 2, 3, 4, and 7, was there treatment with sufficient injections of antimony potassium tartrate, while in Cases 5, 6, and 8 there was treatment with stibophen and Stibanose (diethylaminoethanol salt of sodium antimony gluconate) intramuscularly, because of the unusually small cubital veins in Case 5, with the development of local phlebitis after a few antimony potassium tartrate injections and the presence of coronary sclerosis as revealed by the electrocardiogram in Cases 6 and 8.

4. While three injections of antimony potassium tartrate a week have been found to cause a rapid regression of the lesions in cases of mycosis fungoides in which response was obtained, massive doses of antimony for a short period of time may have given good results in the cases in which the response was poor or in which there was no response at all to moderate doses of antimony potassium tartrate.

Taking into consideration the above qualifications, the histologic structure of Case 1 (Fig. 2) can then be used as a standard for comparison with that of normal tissue (Fig. 1), because this patient with extensive generalized tumors and ulcerations responded rapidly to antimony potassium tartrate therapy after failing to respond to various forms of treatment, including several courses of arsenic and x-rays. She had no recurrences since May 19, 1947, when she so

27. Herzberg, J. J., and Ueberschär, K. H.: Die Mykosis fungoides als neoplastische Erkrankung des erweiterten retikuloendothelialen Systems, Dermat. Wchnschr. **123**:316, and 337, 1951.

28. Garb,[1] p. 306.

29. Garb, J.: Mycosis Fungoides (Granuloma Fungoides), Tumor Stage, Responding Rapidly to Antimony Preparations: Preliminary Report, J. Invest. Dermat. **10**:43 (Feb.) 1948. Garb.[2]

30. Garb,[1] p. 304.

31. Berkovsky, M.: Mycosis Fungoides Treated Successfully with Ethylstibamine (Neostibosan), Arch. Dermat. & Syph. **61**:686 (April) 1950.

dramatically responded to treatment with 10 intravenous injections of antimony potassium tartrate, and has been free of lesions since Nov. 22, 1948. The response to treatment in this case corresponds to the good cellular and reticulum hyperplasia.

In Case 2, the patient, with generalized nodular and infiltrated growths of six months' duration, had likewise shown the dramatic result of antimony potassium tartrate treatment. She had no recurrences since she began to respond to treatment with antimony potassium tartrate on Dec. 10, 1947, and has been completely free of lesions from May 9, 1948, until her last examination on Jan. 8, 1952. This patient had a response similar to the response in Case 1. The less pronounced cellular infiltration and increase in reticulum fibers (Fig. 3) may be attributed to the short duration (only six months) of the lesions.

In Case 3 a rapid regression of the lesions proportional to the cellular and reticulum hyperplasia was also shown. The more extensive cellular infiltration and increase in reticulum fibers, greater than that shown in Case 2, may probably be due to the longer duration of the lesions. The failure of all the lesions to regress may be attributed to the discontinuance of the antimony potassium tartrate therapy after 16 injections because of myocardial involvement.

In Case 4 only a moderate response in the infiltration and in the reticulum was shown. There was only a partial regression of the lesions. A better response to antimony was anticipated, but perhaps the patient's age, 75 years, and the large intra-abdominal tumor, from which the patient subsequently died, were factors overcoming the defense mechanism. The nature of this tumor was not determined, because an autopsy was not permitted.

Case 5, in which there was no response to the antimonial therapy, parallels the fairly poor perivascular cellular infiltration and the poor reticulum hyperplasia (Fig. 4). This patient was later treated with nitrogen mustard, with unfavorable results. She died soon after receiving cortisone therapy.

The mild response to antimony therapy in Case 6, notwithstanding pronounced cellular infiltration and the moderate reticulum hyperplasia (Figs. 5 and 6) may perhaps be attributed to the cardiovascular complications necessitating the use of stibophen and Stibanose, the milder antimony preparations. This patient, a woman aged 61, had extensive nodular and infiltrated patches of 22 months' duration, with uncontrollable itching. She died a few months later from cardiovascular and renal complications.

In Case 7 there were generalized infiltrations and tumors of six months' duration. The patient received at first 20 antimony potassium tartrate injections and later stibophen and Stibanose injections. This patient showed encouraging results, which at first corresponded to the good cellular infiltration and moderate reticulum hyperplasia, but later pneumonia, acute myocarditis with pleural effusion, developed, and he died. The short duration of the lesions appears to have been a deciding factor in the fatal outcome, the disease process overwhelming the still inadequate and rapidly formed defense mechanism.

In Case 8, the patient, a man aged 44, had generalized lesions of 17 years' duration. They consisted of superficial crusted infiltrated patches and nodular growths. He showed only a slight response to the treatments. The fairly good cellular infiltration and reticulum hyperplasia can be attributed to the long duration of the lesions. However, the necessity of treatment with the milder antimony preparations of Stibanose and stibophen because of myocardial involvement probably prevented better therapeutic results. This patient died suddenly from coronary thrombosis on Dec. 17, 1951.

In Case 9,[3] the patient, a woman aged 51, presented, on Nov. 27, 1948, lesions of two months' duration. There were infiltrated patches on the trunk, which later became generalized, some of the growths becoming fungating. There was a rapid response to antimony lithium thiomalate treatment, parallel to the good cellular infiltration and reticulum hyperplasia, after there had been failure to respond to adequate exposures of x-rays. The use of antimony lithium thiomalate, a very powerful and toxic antimony compound, would have to be evaluated in other cases of mycosis fungoides and compared with results of the antimony preparations used in the other eight cases.

In Case 10, the patient, a Negro woman aged 34, had lesions of five years' duration. On June 13, 1951, she presented generalized pruritic infiltrated patches. She was previously treated with six courses of x-rays and with numerous sodium arsenate injections, without appreciable

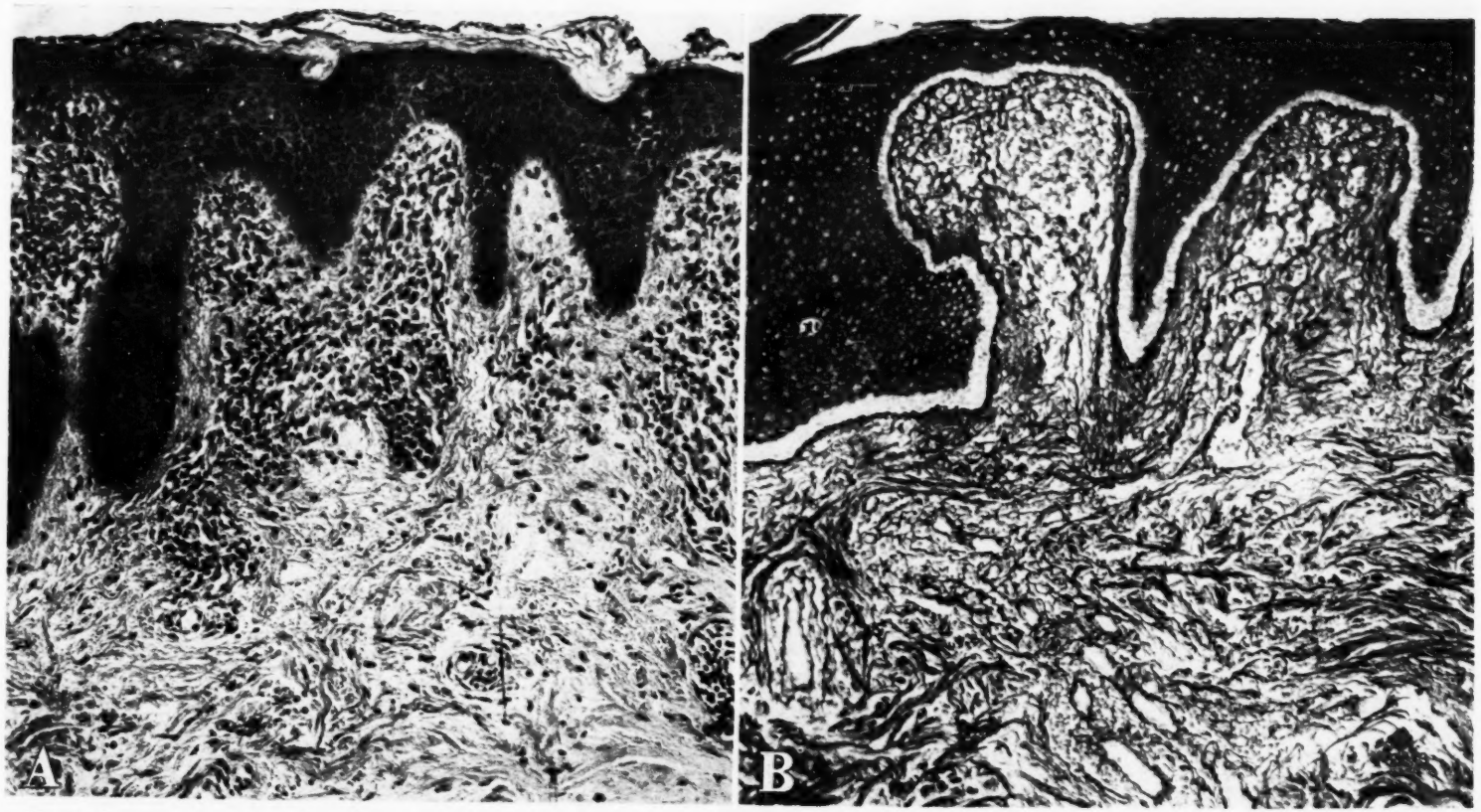

Fig. 6 (Case 6).—*A*, section taken March 4, 1947, showing less amount of infiltration than that shown in Figure 5 *A* (hematoxylin-eosin). *B*, a corresponding diminution in the reticulum fibers as compared with that shown in Figure 5 *B* (reticulum stain); × 157.5

benefits. Twenty-two antimony potassium tartrate injections produced neither alteration in the lesions nor diminution in the itching. The histologic section revealed a good reticuloendothelial cell hyperplasia and a corresponding increase in reticulum fibers.

In Case 11, the patient, a woman aged 44, had lesions of 10 years' duration. Most of the tumors, however, appeared suddenly in November, 1951. She presented generalized various-sized tumors up to the size of small tomatoes, many of which were ulcerated. Some tumors seemed to have undergone partial regression, but as a whole the response was negative to 15 antimony potassium tartrate injections. The histologic section revealed a good cellular infiltration and an increase in reticulum fibers. The sudden generalized appearance of the tumors three months before the treatment with antimony potassium tartrate injections indicates either a weakening or an overpowering of the defense mechanism.

Our present investigation was stimulated by the report of Henstell and his co-workers [32] on six patients with mycosis fungoides treated with nitrogen mustard. They found a direct correlation between the clinical improvement and the number of the reticuloendothelial cells. Thus, three patients who showed the best response had a high incidence of reticuloendothelial cells, while three other patients who responded the least had a low percentage of these cells. In the 11 cases herewith presented, four patients responded and seven patients did not react to the antimonials, despite the fact that in six of the seven patients there was a decided reticuloendothelial cell hyperplasia. Only one patient disclosed a poor cellular and reticulum hyperplasia paralleling the unfavorable response to antimonials. Perhaps the cases in which there was no reaction could be explained on grounds such as the varied complications encountered, with the necessity of resorting to milder antimonials, as in Cases 4, 6, and 8, the short duration of the lesions, as in Case 7, and the rapid dissemination of the tumors, as in Case 11, which would signify an overwhelming of the defense mechanism of the body. But whether these explanations suffice to account for lack of response is still a question, and we must at present conclude that there is no proof of a positive correlation between reticuloendothelial cell hyperplasia and the response of mycosis fungoides to antimonials.

It is worth mentioning the statement of Jaffee,[33] that mycosis fungoides is characterized by pronounced eosinophilia and the comment by Winer [34] that "it seems that the more malignant the mycosis fungoides the fewer the number of eosinophils." In the 11 cases herewith reported the infiltrations showed either no eosinophiles or very few eosinophiles. Apparently the number of eosinophiles had no prognostic value and seemed to have no bearing whatsoever on the effectiveness of the antimonials. It is also worthy of comment that the number of the so-called mycosis cells did not appear to have a direct relationship to the result of treatment with the antimonials.

How the time element plays a part in the reticuloendothelial cell response is shown by the smaller amount of infiltration and reticulum fibers in the section in Case 6 (Fig. 6) taken 7½ months earlier.

32. Henstell, H. H.; Tober, J. N., and Newman, B. A.: The Influence of Nitrogen Mustard on Mycosis Fungoides: Observations Relating Its Effect to Reticulo-Endothelial System, Blood **2**:564 (Nov.) 1947.

33. Jaffee,[5] p. 1107.

34. Winer, L. H.: Mycosis Fungoides: Benign and Malignant Reticulum Cell Dysplasia, Arch. Dermat. & Syph. **56**:480 (Oct.) 1947.

SUMMARY

Histologic studies were made of the cellular infiltrations and reticulum fibers of 11 cases of mycosis fungoides, with reference to the possible relationship of reticuloendothelial cell hyperplasia to the response of mycosis fungoides to antimonials. These studies were stimulated by Henstell and his associates, who found a direct relationship in three out of six cases of mycosis fungoides in which there was treatment with nitrogen mustard between the clinical improvement and the reticuloendothelial cell hyperplasia.

Only qualitative studies could be made for two reasons: First, this series consisted of a mixed group in various stages of mycosis fungoides. (A better index would be one in which there was a more uniform group of patients in tumor and ulcerative stages of long duration.) Second, because of complications only milder antimony preparations had to be used in two cases.

In 4 of the 11 cases studied there was a good response to antimonial therapy, while in 7 there was no response, despite the fact that in 6 of the 7 cases there was a decided reticuloendothelial cell hyperplasia. Only one case in which there was an unfavorable reaction to antimonials, a parallel poor reticuloendothelial cell hyperplasia was disclosed. Perhaps the cases in which there was no reaction could be explained on grounds such as varied complications encountered and rapid dissemination of tumors, which would signify an overwhelming of the defense mechanism of the body. Whether these explanations suffice to account for lack of response is still a moot point, and for the present it must be concluded that there is no proof of a positive correlation between reticuloendothelial cell hyperplasia and the response of mycosis fungoides to antimonials.

There seemed to be no relationship between the number of so-called mycosis cells and eosinophiles in the infiltrations and the response to the antimonials. There were no eosinophiles or only an occasional eosinophile.

The time element apparently plays a part in the extent of the cellular infiltration and reticulum fibers, as shown by the differences in reticuloendothelial cell hyperplasia in two sections taken 7½ months apart in Case 6.

A review of the reticuloendothelial system, the histologic structure of mycosis fungoides, and special studies of reticulum fibers have been included.

In relation to the general question of therapy in this disease, it should be mentioned that other antimony preparations may prove even more effective than antimony potassium tartrate (tartar emetic), which thus far appears to one of us (J. G.) to be the most effective in cases of mycosis fungoides in which there is a response to antimony therapy. Moreover, the result may depend upon the method of administration. Perhaps massive doses for a short period may produce results in cases in which the routine treatment of three injections a week of 5 cc. of 1% solution of antimony potassium tartrate or stibophen (Fuadin) fails to cause regression of the lesions.

219 E. 19 St.

1840 Grand Concourse.

CLINICAL EVALUATION OF TOPICALLY APPLIED ESTROGEN CREAM IN ACNE VULGARIS

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IT IS GENERALLY agreed that hormonal influence on the pilosebaceous apparatus is the causative or a contributing factor in the production of acne vulgaris. The androgenic hormones are most commonly incriminated.[1] This is based on the observations that (1) acne usually begins at puberty, when there is increased hormonal activity, (2) acne does not develop in eunuchs, (3) the administration of androgens to castrated men and to women with normal skins may produce acne lesions, (4) when the androgens are no longer given to the eunuchs and to women with normal skins the acne lesions disappear.

Reports have appeared in the literature showing that the topical application of sex hormones has produced histologic changes in the sebaceous glands of animals.[2]

Moreover, the therapeutic effectiveness of systemic administrations of various types of estrogenic materials in some cases of acne vulgaris has now been established.[3]

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1. (*a*) Sulzberger, M. B., and Witten, V. H.: Symposium on Diseases of the Skin: Hormones and Acne Vulgaris, M. Clin. North America **35**:373-390 (March) 1951. (*b*) Barber, H. W.: The Influence of Sex Hormones on the Skin and Pilosebaceous System, in Modern Trends in Dermatology, edited by R. M. B. MacKenna, New York, Paul B. Hoeber, Inc., 1948, Chap. 6, pp. 112-115. (*c*) Hamilton, J. B.: Male Hormone Substance: A Prime Factor in Acne, J. Clin. Endocrinol. **1**:570-592 (July) 1941.

2. Reiss, F., and Gellis, S.: Effects Produced on Pilosebaceous System and Adrenals of Rabbit by Inunction of the Sex Hormones, J. Invest. Dermat. **12**:159-172 (March) 1949. Hooker, C. W., and Pfeiffer, C. A.: Effects of Sex Hormones upon Body Growth, Skin, Hair, and Sebaceous Glands in the Rat, Endocrinology **32**:69-76 (Jan.) 1943.

3. Year Book of Dermatology and Syphilology, edited by M. B. Sulzberger, and R. L. Baer, Chicago, The Year Book Publishers, Inc., 1949, pp. 9-39. Goldzieher, M. A.: Endocrine Pathogenesis and Treatment of Acne Vulgaris, M. Rec. **160**:725-727 (Dec.) 1947. Goeckerman, W. H.: Hormonal Therapy of Acne Vulgaris in the Female: Clinical Attempts at Its Evaluation, Arch. Dermat. & Syph. **61**:237-243 (Feb.) 1950. Sulzberger, M. B., and Wolf, J.:

(Footnotes continued on next page)

Recently, reports of encouraging results in the treatment of acne vulgaris with the local inunction of an estrogen cream have been published.[4]

This study was undertaken in order to evaluate further the clinical efficacy of such topical applications of estrogen-containing creams in the treatment of acne vulgaris.

MATERIALS AND METHODS

To one side of the face approximately 1 gm. of cream base containing 2.5 mg. of water-soluble conjugated estrogen substances (equine) (Premarin cream)[5] was rubbed in once daily at bedtime. To the other side of the face the estrogen-free cream base (used as a control) was applied in a like manner. On arising the next morning the patient washed his face with ordinary toilet soap, and no other treatment was given. The patient did not know which was the active and which was the control cream.

Thirty patients at the skin and cancer unit of the University Hospital, New York University Bellevue-Medical Center, were selected for this study. Four of the patients did not return after treatment was instituted. The other 26 patients were followed for a period of 2 to 16 weeks. There were 17 female patients and 9 male patients. Their ages ranged from 13 to 29 years. The total amount of hormone applied on the one side of the face ranged from 38 mg. to 204 mg.

RESULTS

The results are divided into five groups, the grouping depending on whether the improvement on the side of the face treated with the hormone cream was "great," "moderate," "slight," "not discernible," or if the acne was made worse.

Group 1 (Great Improvement).—In three of the patients there was great improvement of the side of the face treated with the estrogen cream and a moderate degree of improvement on the side treated with the control cream. All were male patients who had large cystic lesions.

Group 2 (Moderate Improvement).—Six female patients and one male patient showed a moderate degree of improvement on both sides of the face. Two female patients had a moderate degree of improvement with the active cream, while the control side showed slight improvement in one and no improvement in another patient. The predominant lesions in these patients were papules and pustules.

One female patient with cystic acne showed a moderate degree of improvement with the estrogen cream. No control cream was used.

Group 3 (Slight Improvement).—Three female patients and one male patient showed slight improvement on both sides of the face. One female patient had slight improvement on the side treated with the hormone and a moderated degree of improvement on the control side. The predominant lesions in these five patients were papules and pustules.

One male patient with cystic lesions had a slight degree of improvement on both sides of the face.

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4. Shapiro, I.: Estrogens by Local Application in the Treatment of Acne Vulgaris, A. M. A. Arch. Dermat. & Syph. **63**:224-227 (Feb.) 1951. Whitelaw, M. J.: Treatment of Adolescent Acne with Topical Application of Estrogens, J. Clin. Endocrinol. **11**:487-491 (May) 1951.

5. The Premarin cream was supplied by Ayerst, McKenna, & Harrison, Ltd., Dr. John B. Jewell, Medical Director.

Group 4 (Improvement Not Discernible).—Two female and three male patients showed no discernible improvement on either side of the face. The predominant lesions were papules and pustules.

Results of Treatment with Estrogen Cream

Patient	Age	Sex	Duration of Acne, Yr.	Predominant Acne Lesion	Weeks of Treatment	Results	
						Active Ointment	Control Ointment
M. K.	18	M	3	Cystic	14	Great improvement; old lesions underwent involution, but new cystic lesions developed during treatment	Moderate improvement; lesions underwent involution, but at a slower rate
P. H.	18	M	13	Cystic	15	Great improvement	Moderate improvement
T. H.	14	M	1½	Cystic	11	Great improvement	Moderate improvement
A. Z.	18	M	2½	Papules, pustules	9	Moderate improvement	Moderate improvement
M. H.	20	F	13	Cystic	9	Moderate improvement	No control used
C. G.	18	F	7	Papules	13	Moderate improvement	Moderate improvement
J. A.	19	F	⅝	Papules, comedones	13	Moderate improvement	Slight improvement
D. K.	18	F	1	Papules, pustules	4	Moderate improvement	Moderate improvement
E. A.	20	F	7	Papules, pustules, comedones	3	Moderate improvement	No discernible improvement
S. P.	13	F	3	Papules, pustules, comedones, cysts	6	Moderate improvement	Slight improvement
G. N.	20	F	8	Papules, pustules, comedones, cysts	2	Moderate improvement	Moderate improvement
A. R.	20	F	6	Papules, cysts	3	Moderate improvement New lesions developed one week prior to menses	Moderate improvement
C. F.	17	F	4½	Papules, pustules	10	Moderate improvement Flare-up three days after menses	Moderate improvement
A. M.	20	F	3	Papules, cysts	16	Slight improvement	Slight improvement
M. C.	28	F	7	Papules, pustules	6	Slight improvement New lesions developed one week prior to menses	Slight improvement
A. F.	23	M	4	Papules, pustules	2	Slight improvement	Slight improvement
M. Co.	21	F	2	Papules, pustules	6	Slight improvement	Slight improvement
R. Ru.	26	F	3	Papules, pustules	4	Slight improvement	Moderate improvement
S. W.	14	M	1½	Cystic	5	Slight improvement	Slight improvement
L. B.	16	F	3½	Papules, pustules, comedones, cysts	2	No discernible improvement	No discernible improvement
M. G.	21	M	3	Papules, pustules, comedones, cysts	2	No discernible improvement	No discernible improvement
R. R.	19	M	5	Papules, cysts	4	No discernible improvement	No discernible improvement
R. J.	15	F	¼+	Papules, pustules	2	No discernible improvement	No discernible improvement
A. B.	23	F	8	Pustules	2	No discernible improvement	No discernible improvement
P. R.	19	M	7	Papules, pustules, comedones	5	No discernible improvement	No discernible improvement
L. S.	18	F	5	Papules, pustules	3	Acne became worse on both sides; edema and erythema developed on the side treated with the active ointment; there was slight erythema on the side treated with the control base. (This may have been an allergic eczematous contact dermatitis. The patient refused to take patch test for the various components of the ointment.)	.....

Group 5 (Worse).—In one girl with papular and pustular lesions many more such lesions developed on both sides of the face while she was under treatment. The side of the face treated with the hormone became edematous and erythematous. The side treated with the control cream had slight erythema.

COMMENT

It is of interest to note that the three patients who showed great improvement on the side treated with the hormone were male patients with numerous large fluctuant cystic lesions. Though the large cystic lesions regressed, new cystic lesions developed which appeared to be smaller and fewer, and which developed more slowly.

Similar results have been reported in the treatment of cystic acne in male patients by the oral and intramuscular administration of estrogens, and by the subcutaneous implantation of estrogen pellets.[6]

In the patients in which the predominant acne lesions were papules and/or pustules the results were either not striking, or there was no discernible improvement.

We had the impression that the cream vehicle itself tended to maintain the excessive oiliness of some skins.

As a rule, when the papular and pustular acne lesions improved, the improvement was noticeable after about two weeks of therapy. Prolongation of the treatment did not usually increase the degree of improvement.

The erythema and swelling that developed in one patient on the side treated with the hormone cream may have been the result of an allergic eczematous contact dermatitis. The patient, however, refused to take patch tests for the various components of the cream.

None of the patients showed evidence of systemic absorption of the estrogen. There was no alteration of the menses, no nipple tenderness, and no gynecomastia.

The influence of the menses upon the acne lesions was unchanged by the topical application of the estrogen cream.

It was an interesting observation that—in all but one case—when improvement took place on the side treated with the estrogen cream, a variable degree of improvement also took place on the side treated with the control base. The following three possible explanations for this phenomenon can be enumerated.

1. There may have been an accidental spread of the estrogen cream to the side treated with the control cream.

2. There may have been systemic absorption of the estrogen. (However, all signs of systemic effect were lacking, and acne lesions on the back and chest, which were not treated topically, did not improve.)

3. This may be an example of "therapeutic shock" on the untreated side, as expressed by H. W. Siemens.[6]

SUMMARY

Twenty-six patients were treated on one side of the face with approximately 1 gm. of cream base containing 2.5 mg. of water-soluble conjugated estrogen substance (equine) (Premarin) once daily. To the other side of the face an estrogen-free control cream was applied.

Great improvement of the hormone-treated side was noted in three male patients with large cystic lesions. Patients with papular and pustular lesions had moderate, slight, or no discernible improvement on the side treated with the estrogen cream.

6. Siemens, H. W.: Über ein noch nicht beschriebenes Phänomen bei der einseitigen Behandlung von Hautkrankheiten, Hautarzt **2**:439-442 (Oct.) 1951.

ANGIOKERATOMA CORPORIS DIFFUSUM

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ANGIOKERATOMA corporis diffusum is only rarely described in the usual textbooks. This is not surprising, since only about 20 characteristic cases of angiokeratoma corporis diffusum have been observed since its first description in 1898. However, it would be wrong to consider this skin condition a dermatological curiosity. Investigations during the past few years have shown that in all probability this cutaneous anomaly will have to be considered as a sign of an internal disease unknown so far. It is by no means inconceivable that the rarity of angiokeratoma corporis diffusum (as far as I know, no case has yet been described in America) is due to the fact that remarkably few dermatologists seem to be familiar with this condition. The purpose of this paper is to draw attention once more to the skin disorder concerned. At the same time, a description of the internal anomalies which have recently been observed in a number of cases will be given, including an account of my own investigations.

Angiokeratoma corporis diffusum was first described by Fabry,[1] in 1898, under the extremely inappropriate name of "purpura hemorrhagica nodularis." The cutaneous lesions consist of very small efflorescences, only slightly hyperkeratotic, or not so at all, as opposed to angiokeratoma Mibelli. They are more or less disseminated on the body (particularly the trunk and extremities) and do not disappear on diascopic pressure. The exanthem consists of small to very small (pinhead-sized) spots or slightly elevated papules. Their color varies from purple to dark blue-red, becoming leaden-hued to black later. Less characteristic, somewhat larger papular lesions (on the scrotum, for example), may also be observed. Involvement of the mucous membranes is rare. Histologically, the skin chiefly shows a considerable dilatation of the capillaries supplying the papillae, resulting in lacunar spaces filled with blood. As a rule, these are observed just below the epidermis and sometimes seem to be surrounded by the rete. More deeply situated vessels may also be involved.

Koch [2] and Weicksel [3] observed ampulla-like dilatations of the conjunctival and retinal blood vessels in patients suffering from angiokeratoma corporis diffusum.

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1. Fabry, J.: Ein Beitrag zur Purpura haemorrhagica nodularis, Arch. Dermat. u. Syph. **43**: 1898.

2. Koch, H., cited by Hornbostel, H.; Spier, W., and Koch, H.: Angiokeratoma corporis diffusum universale (Fabry) mit cardio-vaso-renalem Symptomenkomplex als Allgemeinerkrankung, Arztl. Wchnschr. **6**:49, 1951.

3. Weicksel, G.: Angiomatosis bzw. Angiokeratosis universalis, Deutsche. med. Wchnschr. **51**:898, 1925.

Fig. 1.—Patient of Fabry with angiokeratoma corporis diffusum (reprinted from Archiv für Dermatologie und Syphilis **43**:1898).

Fig. 2.—Skin, showing spaces filled with blood. Hematoxylin and eosin stain.

The former feels that he has demonstrated an anastomosis between retinal arteries and venules. In a personal observation, a remarkable corneal turbidity was seen upon examination by means of the slit lamp.

Typical cases of angiokeratoma corporis diffusum should be recognized without difficulty if the condition is kept in mind as a possibility. However, it is our experience, especially since more attention is being paid to this affection of late, that the diagnosis is frequently made on insufficient grounds. In this connection, the following points may be of additional aid in establishing the diagnosis. Thus, in angiokeratoma corporis diffusum the eruption, in which a number of elements possess a peculiar bluish-black color, usually shows a highly monomorphous picture. The distribution of the efflorescences (mainly on the trunk and the extremities) should also be considered. In angiokeratoma corporis diffusum the skin lesions develop in the patient at a very early age (before puberty), and, as far as can be judged at present, the affection had so far been observed only in the male sex. Finally, the concurrence of the skin affection with a particular internal disorder, as observed in a number of cases of late, probably will prove to be of considerable importance.

The above-mentioned findings have again drawn particular attention to the skin disorder involved. The following is a brief survey of the facts which led to the disclosure of the concomitant visceral changes.

REPORT OF CASES

In 1939, I was able to examine, together with A. W. M. Pompen,[4] three patients (brothers) with typical cases of angiokeratoma corporis diffusum. These three patients at the same time exhibited a number of signs and symptoms pointing to involvement of the internal organs, namely:

1. Vasomotor disturbances; pains and spasms in the hands, feet, and upper legs, increasing at higher temperatures and abating under the influence of cooling (one of the patients, moreover, had a disturbed sweat secretion).

2. Edema of many years' standing, chiefly localized in the feet and the lower parts of the legs (no cardiac failure or renal insufficiency; normal protein spectrum of blood plasma).

3. Moderately but constantly raised blood pressure.

4. Cardiac enlargement, particularly of the left ventricle.

5. Urinary abnormalities; slightly to strongly positive albuminuria; in the sediment always a few erythrocytes and leucocytes, and often a few casts.

The cause of the above abnormalities remained unaccounted for. Pathological changes in the blood vessels were considered. The signs and symptoms cited were summarized under the name of cardiovascular-renal symptom complex.

In 1944 one of the patients mentioned above died at the age of 37 in uremic coma. The postmortem examination, incomplete owing to war conditions, was performed with the cooperation of Dr. H. J. G. Wyers, pathologist at the Hague. The most striking changes were found in the

4. Ruiter, M., and Pompen, A. W. M.: Angiokeratoma corporis diffusum (universale) mit kardiovasorenalem Symptomenkomplex bei 3 Brüdern, Arch. Dermat. u. Syph. **179**:165, 1939. Ruiter, M.: Drie patienten (broers) met angiokeratoma corporis diffusum, Nederl. tijdschr. geneesk. **83**:1801, 1939.

cardiovascular system.[5] The walls of the blood vessels (kidneys, adrenal glands, liver, spleen, lungs, heart, and skin) were greatly thickened, this being chiefly due to a marked broadening of the media. The cells of the muscle layer (eosin-hematoxylin stain) were considerably swollen and did not stain well; their nuclei were broad and often highly polymorphous, and their proto-

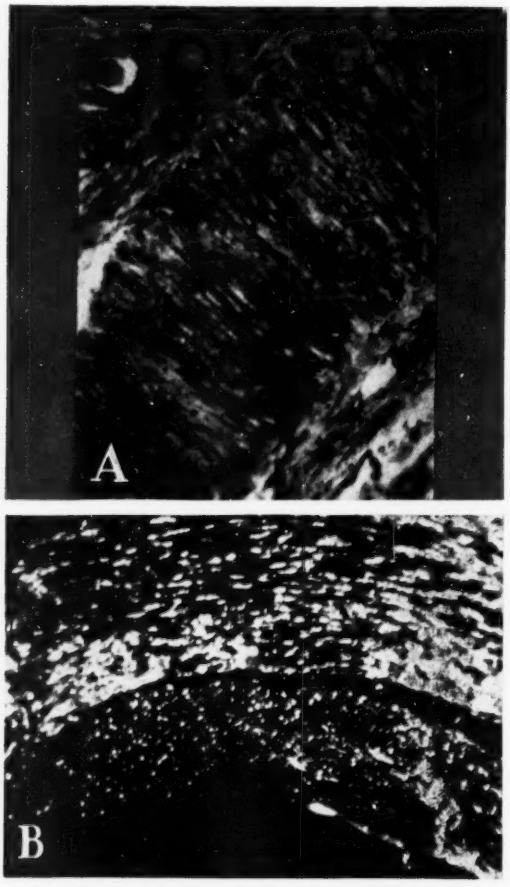

Fig. 3.—*A*, hematoxylin and eosin stain. Tangential section of middle-sized artery showing swollen muscle cells of the media with vacuolation (personal observation). *B*, cross section of middle-sized artery (polariscopic examination). The vacuolated muscle cells of the media are filled with a doubly refractile substance. There is thickening of the intima, with scattered fat droplets (Scriba's case).

5. Ruiter, M.; Pompen, A. W. M., and Wyers, H. J. G.: Über interne und pathologisch-anatomische Befunde bei Angiokeratoma corporis diffusum (Fabry), Dermatologica **94**:1, 1947. Pompen, A. W. M.; Ruiter, M., and Wyers, H. J. G.: Angiokeratoma corporis diffusum (universale) Fabry, as a sign of an unknown internal disease: Two autopsy reports, Acta med. scandinav. **128**:234, 1947. Ruiter, M.: Angiokeratoma corporis diffusum (universale) als symptoom van een onbekende en nog niet beschreven inwendige ziekte, Nederl. tijdschr. geneesk. **90**:1757, 1946.

plasm was vacuolated, the vacuoles which were spindle-shaped lying mostly beside the nuclei. The muscle fibers of the heart (450 gm.) showed completely identical changes, in particular obvious vacuolation. On cross section they had an annular aspect.

As a hypothesis, the existence of a storage disease was suggested, assuming that the vacuolation was caused by storage in the muscle cells of a substance undemonstrable by the staining methods used.

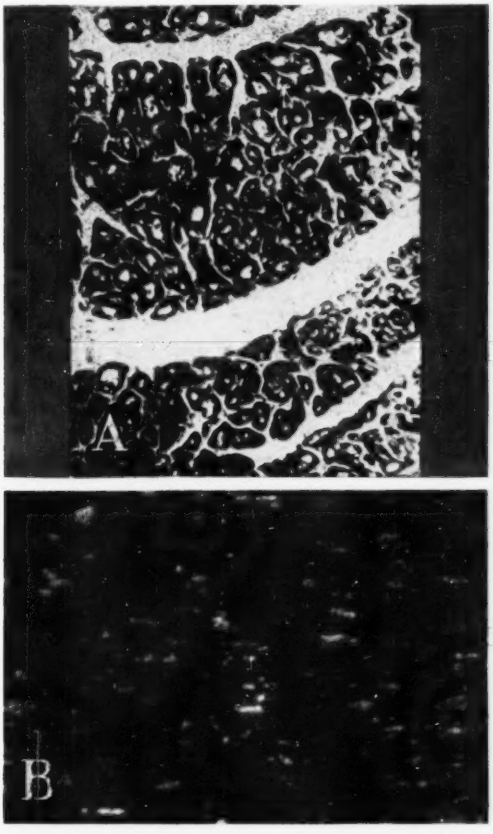

Fig. 4.—*A*, hematoxylin and eosin stain. Cross section of the cardiac muscle. Ringform of vacuolated muscle fibers (personal observation). *B*, longitudinal section of cardiac muscle (polariscopic examination). Muscle fibers with elongated vacuoles containing a doubly refractile product (Scriba's case).

The same vascular and cardiac changes were observed in microscopic slides of another case of angiokeratoma corporis diffusum (Dr. Kooy, Amsterdam), in which the patient had also shown during life the group of signs and symptoms enumerated above and had died from uremia. When studying the literature I was moreover struck by the fact that the majority of the patients, though mostly insufficiently examined, had shown one or more signs or symptoms of the cardiovasorenal symptom complex. For these reasons, I felt justified in assuming that there was a relationship between the cutaneous anomaly and the internal disorder.

In 1950, Scriba,[6] of Hamburg, performed an autopsy on a patient (a 46-year-old man) with typical angiokeratoma corporis diffusum, who during his lifetime had shown the cardiovascular-renal symptom complex and had died of cardiac infarct.[7] Initially, he found the same changes in the cardiovascular system (vacuolation, etc.) as those described by my co-worker and myself. He later succeeded in staining (faintly yellow-red with hematoxylin and scarlet red) the stored product, which we had assumed to be present. The contents of the vacuoles proved to be doubly refractile too. Scriba also found this substance in the ganglion cells of the brain and the peripheral nervous system. He demonstrated it further in foam cells, which were observed in the lymph nodes and the spleen, for instance.

The investigations of Scriba therefore showed that the pathological findings were based on an unusual form of lipid metabolic disturbance (lipid thesaurismosis). In this way our original hypothesis was confirmed. The phosphatide in question was more closely investigated by Kühnau (Hamburg). Up to now, it appears that it probably largely consists of a diaminophosphatide. It is related to sphingomyelin, but is distinguished from real sphingomyelin by differences in solubility, among other points.

Wertheim [8] at the time concluded that angiokeratoma corporis diffusum should be considered a form of angiomatosis. He formed this opinion mainly on the strength of the histopathological picture. I disagree with his views, and I am of the opinion that the arguments advanced by him are not conclusive. In addition, my own histopathological investigations failed to confirm a number of the histopathological changes emphasized by Wertheim.

In my opinion, the essential pathological process in angiokeratoma corporis diffusum consists in dilatation of preexistent vessels, in which the capillaries of the strength of the histopathological picture. I disagree with his views, and I am of the opinion that the arguments advanced by him are not conclusive. In addition, my of vascular tonus, caused by the changes observed in the muscular coat of the blood vessels, has been of importance. The vasomotor disturbances, arising from the pathological changes of the peripheral ganglion cells, may have contributed to the dilation of the capillaries of the papillary layer too.

The most important points of diagnostic value in angiokeratoma corporis diffusum have been mentioned already. In view of the rarity of this clinical picture and the fact that it is little known among dermatologists, a discussion of the differential diagnosis seems desirable.

Angiokeratoma corporis diffusum must be differentiated from Rendu-Osler disease, among other affections, and, in particular, from the atypical forms sometimes observed. In angiokeratoma corporis diffusum the skin of the trunk is always affected, with a certain preference for the areas of predilection, as seen in seborrheic dermatitis. In Rendu-Osler disease the efflorescences occur mainly on the face and on the adjoining mucous membranes. They are also sometimes found on the trunk, but then they are chiefly localized on the upper part of the chest and on the distal parts of the arms. The cutaneous lesions in Rendu-Osler disease show a highly polymorphous appearance (punctate and ordinary telangiectasis, small angiomas, angiomas of the nevus araneus type, etc.). This is in contradistinction to the more

6. Scriba, K.: Zur Pathogenese des Angiokeratoma corporis diffusum Fabry mit cardiovasorenalem Symptomenkomplex. Verhandl. deutsch. Gesellsch. Path. 1950, p. 221.

7. Hornbostel, H.; Spier, W., and Koch, H.: Angiokeratoma corporis diffusum universale (Fabry) mit cardio-vaso-renalem Symptomenkomplex als Allgemeinerkrankung, Arztl. Wchnschr. **6**:49, 1951.

8. Wertheim: Hämangiome, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Springer-Verlag, 1932, Vol. 2.

monomorphous appearance of the skin eruption in angiokeratoma corporis diffusum, in which leaden-hued to black lesions frequently are a conspicuous feature. The time of appearance is also clearly different in the two affections. As a rule, the manifestations of Rendu-Osler disease occur during puberty or in women in the climacteric. In angiokeratoma corporis diffusum the cutaneous lesions in general develop at a very early age (before puberty). The tendency toward profuse hemorrhages from the mucous membranes is pathognomonic for the Rendu-Osler syndrome. This sign is rare or absent in angiokeratoma corporis diffusum. It is worth mentioning that angiokeratoma corporis diffusum, of which some familial cases have been described, has so far, to our knowledge, only been observed in the male sex. Rendu-Osler disease, however, occurs in both sexes.

Disseminated telangiectases (usually of the nevus araneus type) as seen in diseases of the liver should also be considered in the differential diagnosis. The same is true for senile angiomas, which may occur in great numbers on the trunk. Angioma serpiginosum and forms of generalized angiomatosis may lead to misdiagnosis. Usually, it will not be difficult to distinguish these affections from angiokeratoma corporis diffusum.

The term "angiokeratoma" is also used for a number of other skin disorders. The individual lesions in angiokeratoma corporis diffusum may show a certain similarity to the efflorescences observed in these affections. Probably, the rather inappropriate name for the disease used at present must be attributed to this fact. Skin affections, also indicated by the term angiokeratoma, are: angiokeratoma Mibelli, angiokeratoma scroti, and angiokeratoma neviforme. They should be sharply distinguished from angiokeratoma corporis diffusum, not only on the basis of clinical and morphological properties, but in particular because their pathogenesis probably is quite different from that which I think I am justified in assuming in angiokeratoma corporis diffusum. A further discussion of angiokeratoma Mibelli and scrotal angiokeratoma is superfluous, as these clinical pictures are sufficiently known. In angiokeratoma neviforme (circumscriptum) the efflorescences are usually limited to one or more regions of the integument (e. g., to the buttocks, legs, and scrotum). The lesions are sometimes band-shaped; they may show a unilateral distribution, and there is possibly a diffuse form. Angiokeratoma neviforme belongs to the group of the angiomatous nevi and thus is essentially a nevoid affection of the skin.

As was said in the beginning of this article, angiokeratoma corporis diffusum has so far remained an extremely rare and therefore little-known clinical picture. However, in the future we shall have to bear in mind that this cutaneous affection may be an important sign of a serious internal disease. This is of even greater importance in that the general clinical examination does not give sufficient indications of the existence of the disturbance of the phosphatid metabolism discussed. Whether all cases of angiokeratoma corporis diffusum are associated with this type of lipid metabolic disorder can be judged with certainty only when a more extensive number of reports of thoroughly investigated cases are available. It is worthy of record that Hornbostel and Scriba (in a personal communication) have recently again diagnosed a similar case of angiokeratoma corporis diffusum. The accompanying lipid metabolic disorder was confirmed by the findings of a skin biopsy, in which the media of a deeper situated vessel of the muscular type showed the characteristic changes.

CHANGES OF CLIMATE AND ENVIRONMENT IN TREATMENT OF DERMATOLOGIC DISEASES

Effect on Neurodermatitis and Certain Other Chronic Dermatoses

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AND
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IN THE last 15 years there has grown up in the arid portions of the American Southwest a colony of patients with various chronic generalized dermatoses, who have migrated from the colder and more humid portions of the country to take advantage of the sunshine and the warm dry air. It is usually difficult to convince these patients that the benefits they receive can be anything but the effect of the sun and dry air, or that rest and a certain amount of adjustment of their emotional difficulties and a lessening of the drive which has become their way of life plays a part in their recovery. They have become a cult of sunworshippers, and many are overdoing the sun treatment to the extent that they are laying a foundation for the future development of keratoses and epitheliomas.

Our observation of many of these patients and the history of their reactions to various factors before and since coming to the desert country have convinced us that there are other factors involved besides the effects of climate per se. Some of these patients have obtained relief from previous attacks of dermatitis in Florida, Wisconsin, California, and other places and different climates away from home. The desert climate is no safeguard against the development of atopic dermatitis or disseminated neurodermatitis, and it is sometimes necessary to send patients with severe resistant dermatoses which originate in the Southwest away from home before improvement results. In such cases we prefer the seashore as a radical change.

Sulzberger and Garbe,[1] in 1937, described the polymorphous pruritic dermatosis which bears their names and stressed the importance of a change of environment in its treatment. In 1939, Cannon [2] reported eight cases of generalized erythroderma resembling lymphoblastoma in which the lesions cleared up temporarily while the patients were in the hospital, especially if they were in private rooms, but in which the patients were cured only after a prolonged stay in a different climate and environment. He emphasized the benefits of a high, warm, dry

Read at the Seventy-Second Annual Meeting of the American Dermatological Association, Inc., Colorado Springs, Colo., April 25, 1952.

1. Sulzberger, M. B., and Garbe, W.: Nine Cases of Distinctive Exudative Discoid and Lichenoid Chronic Dermatosis, Arch. Dermat. & Syph. **36**:247 (Aug.) 1937.

2. Cannon, A. B.: Allergic Dermatitis Simulating Lymphoblastoma, Arch. Dermat. & Syph. **39**:846 (May) 1939.

climate. These cases probably represented a variety of dermatoses, and their subsequent courses proved them not to be lymphoblastomatous. Later, Sachs and Kirsch [3] reported a series of cases of Sulzberger-Garbe disease in which the lesions cleared up after the patient had taken up residence in Florida or Arizona, whereas they had been resistant to all therapy when the patient was at home in the East. Schneider and Kesten,[4] in 1948, published a study of 10 cases of a lichenoid discoid exudative dermatosis, under the title of polymorphic prurigo. They stated:

> After some months residence in the Southwest away from unsatisfactory emotional environment, seven patients became free from this eruption. Of this group, five have remained in the southwestern states and are ostensibly cured. The other two patients returned to the East, one to her old surroundings, where she has had a recurrence of the eruption, the other to an emotionally satisfactory environment where he has remained well.

The other three patients of their series underwent psychosomatic studies. After therapy, two of the three remained well in their habitual environment.

Eidinoff [5] in a survey of 34 cases of generalized dermatitis (principally atopic dermatitis, disseminated neurodermatitis, and lichenoid discoid exudative dermatosis) from the colder and more humid sections of the country has shown that in a large majority of such cases complete healing or marked improvement was eventually obtained during the patients' residence in the Southwest. In a few of these, however, the healing time was so prolonged that one would hesitate to say that change of climate or any other factor was responsible, excepting a slow, natural subsidence, or "burning out," of the inflammatory process.

The area around El Paso, Texas, the locale of our clinical observations, lies at an altitude of from 3,700 to 4,400 ft. (1.13 km. to 1.34 km.) above sea level, with an average relative humidity of 35%, and an average annual rainfall of approximately 8 in. (20 cm.).

CLASSIFICATION OF CASES

The patients with dermatitis who have been sent to the Southwest and have come under our observation have in common a generalized pruritic dermatitis, intolerance to cold, resistance to the usual therapy, and varying degrees of emotional instability which may be primary or secondary to the disease. These patients may be divided into the following groups:

1. Patients with exudative discoid and lichenoid dermatosis of Sulzberger and Garbe. These patients have almost all improved after periods varying from a few weeks to several years. As a rule, a residence of six months to a year seems advisable before the patients return to their usual work and environment. In some there has been a recurrence soon after their return home; several have made three or four unsuccessful attempts to live in their usual environment. A few have returned home and have remained comparatively well. Since this disease has no specific treatment and since patients fare best in a warm climate, it seems wise to give them the benefit of such a change; however, absence from their usual environment

3. Sachs, W., and Kirsch, N.: Exudative Discoid and Lichenoid Chronic Dermatosis, (Sulzberger-Garbe): Histopathologic Study, J. Invest. Dermat. **8**:215 (April) 1947.

4. Schneider, E., and Kesten, B.: Polymorphic Prurigo: Psychosomatic Study of 3 Cases, J. Invest. Dermat. **10**:205 (March) 1948.

5. Eidinoff, H.: Effect of Environment on Chronic, Severe and Extensive Itching Dermatoses, J. Invest. Dermat. **14**:319 (May) 1950.

should be prolonged, and then a trial trip home is the only way to determine whether a permanent change of residence is necessary. Although disseminated neurodermatitis is a common problem in our practice locally, we have never seen a classic case of Sulzberger-Garbe syndrome in which the disease had developed in the Southwest. We know of no reason for this, unless the combination of a milder climate, the slower tempo of life, and the less aggressive competition in the smaller cities offers a less favorable environment for the development of this dermatosis.

2. Patients with so-called disseminated neurodermatitis. We like to subdivide these into three classes:

(*a*) Patients with classic atopic dermatitis with a history of atopic diseases in the patient or his family. Some of these patients have had repeated episodes of dermatitis, while others had been free of lesions for years until the strain of life and business overwhelmed them in the middle years. These patients have usually had repeated skin tests, and although they often give positive reactions to many allergens, restrictions and trial diets have usually produced very disappointing results. The emotional factor seems to be the most important one, as a rule.

(*b*) Patients with disseminated neurodermatitis appearing first in the adult and without previous history of atopic disturbances.

(*c*) Patients with cases beginning as typical contact dermatitis or seborrheic dermatitis, gradually becoming generalized and lichenified, and assuming the usual characteristics of disseminated neurodermatitis. In the hypersensitive, unstable person this may be the result of domestic and economic situations engendered by the original dermatitis itself, the contact or seborrheic dermatitis acting as a "trigger mechanism" which initiates a neurodermatitis.

These three types present an identical appearance once they have become generalized, and they run a similar course. The patients tend gradually to respond to rest, a warm climate, sunshine, and relaxation, but are subject to exacerbations in cold weather, and especially after emotional upsets, too strenuous work, or unpleasant business experiences, just as they are in their usual environment.

3. Patients with generalized exfoliative dermatitis and erythroderma resulting from psoriasis. Although several of these have been benefited by rest and cautious heliotherapy in the Southwest, one such patient was not improved after several years' stay. Some of these had had relief from previous attacks in Florida, and one after a vacation in Wisconsin.

ROUTINE OF TREATMENT

The majority of these patients who are finally advised to seek a change of climate have already tried almost all the known local and systemic remedies usually prescribed; they are often intolerant to the drugs which one would expect to help the most, and they react best to very mild treatment. The treatment they have received from us has not differed greatly from what they had already received at home, with the exception of the change of environment, the mild dry atmosphere, and sun bathing. In our practice these patients are always cautioned to begin with a very short exposure to the sun, carefully avoiding the slightest reaction. They become enthusiastic about the sun and tend to increase the exposures too rapidly,

with resultant exacerbation of the dermatitis. If the patient's skin tans well we advise him to slowly increase the time until he is taking one hour for each side of the body and then to maintain that exposure. We see no advantage in longer exposures, and on very hot days it is better to divide the exposure time, or to take the sun bathing earlier in the day. Persons with sun-sensitive skin are cautioned to avoid sun bathing, although air bathing in the shade may be permitted both for its psychological effect and for the drying effect on the skin. Sun bathing is not done on cold or windy days.

Patients with obvious major emotional difficulties should have the benefit of the special techniques of the psychiatrist, but many of these people have only an inherent neurovascular instability plus long-continued strain of business worries as the basis of their dermatitis. Others have domestic problems which they themselves must solve before any degree of relaxation is attainable. Although the services of various other specialists are required from time to time, we emphasize the desirability of the patient seeing his dermatologist at regular intervals, both for the treatment of special dermatological situations, such as pyogenic infections and local exacerbations which are common, and in order that the dermatologist may acquire an understanding of the patient's problems; moreover, in this manner, the patient becomes more confident of the physician's interest in his troubles and of his desire to help.

COMMENT

We believe that in all the dermatoses under discussion there is an underlying nervous and vascular instability which varies with the individual person and which causes the skin to react in an exaggerated fashion to various forms of local and emotional stimulation, and that the development of dermatitis in these persons closes the vicious cycle of irritability, increased pruritus, trauma, increased dermatitis, and increased irritability and instability.

When a patent whose disease is basically psychosomatic or who is affected by psychic influences leaves home on vacation, he is placing distance between himself and the domestic and occupational sources of his worries. Relaxation of some degree and a lessening of the tension results, and the longer the patient is away the greater the amount of relaxation, even though the sources of his worries remain unchanged at home. The more complete the change, the better, providing the change is a pleasant one. Many patients with psychosomatic diseases show improvement when they are on a vacation, if the vacation is sufficiently long to encourage this relaxation. Change to a life of slower tempo is beneficial to these patients. Those who have come to the Southwest for treatment of these dermatoses and have brought with them major emotional difficulties, such as business worries and domestic troubles, have, in our experience, not fared well until these difficulties had been in part resolved, or until the patients had had the time to readjust their lives in such a way as to be able to accept the troubles of life without emotional disturbance. We have repeatedly seen rapid improvement result soon after such adjustments were apparent. The businessman who makes a change of climate for his dermatitis and then tries to manage his business in New York by telephone is certainly not going to receive the same benefit from the change as the man who has been able to delegate his work to someone else and to temporarily forget it.

Although any pleasant change of surroundings and climate may be helpful in this group of dermatoses, a mild warm sunny climate seems most beneficial as a rule. A warm sunny beach, preferably in a small community away from crowds, and not sufficiently hot to cause excessive sweating and enervation contributes to a feeling of relaxation and well-being. On the other hand, patients from the low humid sections of the country often experience this "pick-up" most on changing to a moderately high dry sunny climate. An altitude of much over 5,000 ft. (1.52 km.) will sometimes increase the nervousness and sleeplessness of patients who are accustomed to low altitudes. Patients fare best when the weather is pleasant. Cold is poorly tolerated, and many complain of increased nervousness and pruritus during high winds and sand storms. Climatically these patients are perfectionists, and they want and expect the weather to be just right.

The benefits of sun bathing itself are several. Besides the immediate tendency toward relaxation from lying or sitting in the warm sunshine, the effect of the sun on the calcium metabolism possibly lessens the irritability of the skin, and the warmth itself may have an effect in lessening the inflammatory process in the skin, as it does in inflammations elsewhere. The rest periods necessary for sun bathing are undoubtedly helpful to patients who are working; this enforced rest in the middle of the day might have prevented many such dermatoses from developing.

Circulating air, particularly dry air, has a decongestive and dehydrating effect on the skin.

The intense pruritus usually experienced by most patients with this group of dermatoses is perhaps brought about by a combination of influences:

1. The pressure of the edema and cellular infiltrate on the nerve endings.

2. The presence of sweat on the skin surface in early or mild cases, before interference with the sweating mechanism has developed. This is especially uncomfortable in a hot humid climate and is relieved by a climate of low humidity.

3. Retention of sweat, due to inflammatory pressure, or to plugging of the sweat orifices by hyperkeratosis, or by maceration, as suggested by Sulzberger.[6] Dehydration of the skin in a dry climate or as a result of sun and air bathing is a probable factor in relieving this.

4. Emotional influences. In markedly unstable patients, the occasional occurrence of sudden attacks of scratching of an orgasmic character while the patient is rehearsing his troubles to the physician, shows a definite neurotic influence.

We would again caution against overindulgence in heliotherapy in regions such as the Southwest, where the sunshine is intense. In persons who live an outdoor life we see many keratoses and epitheliomas develop at the ages of 30 to 40 years, and in sun-sensitive skins even earlier. We have seen keratoses and one squamous cell epithelioma develop among young patients who were indulging in extensive sun bathing for their dermatitis.

Finally, we suggest that patients who are to seek a change of climate and environment for their dermatoses be advised of the importance of making every effort to minimize any domestic or business sources of worry, and to make financial arrange-

6. Sulzberger, M. B.: The Clinical Significance of Disturbances in Sweat Delivery, Special Lecture, read before the American Academy of Dermatology and Syphilography, Chicago, Dec. 10, 1951.

ments whereby they may feel reasonably sure of living expenses for a stay of six months, or preferably longer, in their new environment. It is our considered opinion that with these arrangements such patients can best attain the state of relaxation which is so important to their improvement.

SUMMARY

While the beneficial effects of a change of environment and of a mild sunny climate on certain chronic generalized dermatoses are recognized, we believe that it would be a mistake to attribute the improvement of these patients to climatic influences alone and to leave the impression that removal to a certain climate, whether it be the seashore or the desert, without attention to the other factors involved, is necessarily followed by a rapid return to health. Many of the patients who have migrated to the Southwest have come with this idea. Change of environment and change of climate appear to be only two of the factors which may be beneficial to these patients. Change of emotional environment, more rest and relaxation, and slower tempo of life are equally important. In spite of the climate of the Southwest, as well as other climates usually considered favorable, this group of dermatoses, when they develop in these portions of the country, remain a problem just as elsewhere unless these other factors receive adequate attention. In this report we have nothing new or original to offer but merely wish to record our impressions, based on a not inconsiderable clinical experience.

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ABSTRACT OF DISCUSSION

Dr. C. W. Lane, St. Louis: Dr. Smith has presented an extremely interesting and valuable paper concerning the treatment of a group of diseases with which he has had a wide experience. For years it has been a general custom of dermatologists in the eastern, northern, and central portions of the United States to send patients with chronic, resistant dermatoses to a warmer drier climate, such as occurs in Arizona, New Mexico, and western Texas. These are the patients whom Dr. Smith has observed for the past 20 years, along with others whose persistent dermatoses began in Texas or in the surrounding territory. It was interesting to note that these persons are in turn referred by Dr. Smith to different locality, preferably the seashore. He believes that patients with eruptions considered to have a neurogenic basis and with other chronic dermatoses respond well to a warm dry climate if in addition they are removed from worries and cares and providing they have the ability to relax and forget their troubles. These conclusions are conservative and have been made after thorough, deliberate observations. He is also performing a valuable service in calling attention to the dangers of prolonged exposure to the sun, with its resultant drying effect and the subsequent appearances of keratoses and cutaneous malignancies. All sun worshippers should heed this warning.

Dr. Smith has grouped together a number of resistant dermatoses which for the most part have responded well to a regimen of climatic change, moderate exposure to sun, rest, and relaxation. Some of these dermatoses are related to each other, and some are distinct entities. All have a common denominator in that to a greater or lesser degree they are related to and affected by the nervous system, but there is a wide variation in opinions concerning the intimacy of this relationship. It is my belief that atopic dermatitis and disseminated neurodermatitis are synonymous terms, whether the eruption occurs in the infant, the adolescent, or the adult. It is a disease which shows a symmetrical involvement most often of the cubital and popliteal regions, the neck and face, but is also often present on the shoulders, axillae, thorax, and wrists. It is characterized by an erythematopapular eruption, which later becomes dry, scaly, thickened, lichenified, hyperpigmented, and excoriated, and which often becomes secondarily infected. It is also a disease

in which emotional influences play some part, but the neurogenic element alone is not sufficient to explain the many variations of the disease. Brandt has aptly stated that there were three main components of the disease, neurogenic features, systemic allergy, and a special response of the skin to diverse stimuli. Atopic dermatitis appears to be unrelated to a seborrheic dermatitis or contact dermatitis which from trauma or overtreatment has become generalized and lichenified. In these diseases not only the areas of involvement and the clinical picture differ from that of atopic dermatitis, but the etiology is not comparable.

Another characteristic feature of disseminated neurodermatitis was revealed by the thorough study of Dr. Engman Sr. and Dr. McArdle, who, employing spectroscopic examination and microincineration, found a magnesium deficiency in the active and healed lesions and in the unaffected skin of these patients. They also discovered that in the inflamed areas there was a deficiency of calcium and silicon, but that when the lesions had healed the calcium and silicon content had returned to normal.

That change of climate is not always essential for the improvement of atopic dermatitis is shown by seasonal variation. A conservative estimate is that in Missouri 90% of the patients with this disease have a spontaneous regression or pronounced clearing in the spring and summer, with recurrence and exacerbation in the fall and winter. Heat and dryness alone are apparently not responsible for this improvement, as there is only a slight variation in the relative humidity in the summer and winter seasons. According to the St. Louis weather bureau the daytime variation is about 10%, which does not seem sufficient to exert such a pronounced beneficial effect on the skin. Likewise, the excessive amount of perspiration which occurs in the hot humid weather of St. Louis aggravates the condition of only a small minority of these patients. The cause of this pronounced seasonal change has not been discovered, but after studying the results of experiments of Dr. Engman Sr. and Dr. McArdle I think it is possible that an important point has been missed, viz., that not the persistent deficiency of magnesium but rather the return of normal values of calcium and silicon in the healed lesions is the important feature. Lending some credence to this opinion is the fact that vitamin D has a mobilizing influence on calcium, and that increased absorption of this vitamin may be one of the reasons why patients improve not only in the summer in St. Louis, but also when they move to the Southwest.

Also, some patients with atopic dermatitis have an abnormal sensitivity to inhalants, contactants, and foods. Among the patients is a high incidence of familial allergy and a history of infantile eczema followed by asthma. These persons, particularly those with a reaction to inhalants, should be helped by change of residence to a warm dry climate.

Patients with atopic dermatitis do have a skin which reacts readily and decidedly to nervous stimuli. High school and college students will often show an exacerbation at examination time, and I have referred students with this disease to Arizona. The condition of most of them has improved while there, but there would be a recurrence on their return home in the winter season. That the climatic change alone did not account for the improvement is shown by the course of a student whose condition had improved in the freshman year and the first semester of his sophomore year. His mother, with whom he was often in emotional conflict at home, moved there with him during the second semester of his sophomore year, and there was a pronounced recurrence of his atopic dermatitis, which persisted until his mother returned to her home in St. Louis. For those tense persons whose atopic dermatitis flares with each emotional upset and who cannot afford a change of environment or who cannot escape from family, relatives, or associates, every effort should be made to reduce the trying episodes and remove the irritating factors.

The avoidance of tension and known allergens, plus the judicious administration of antihistaminics and sedatives, the use of bland, nonsensitizing topical medications, and the careful application of roentgen and actinic rays are the therapeutic methods commonly employed by us. Most patients are helped by this regimen, despite the continuance of home and business irritations and exposure to a climate that none but the most enthusiastic St. Louisan would call ideal. How much nicer for such sufferers if they can flee from their tension and worries to a warm dry climate with abundant sunshine! I heartily agree with Dr. Smith's summary in which he says that change of environment and climate plus rest and relaxation all are helpful in bringing about improvement in this persistent disease.

DR. MARION B. SULZBERGER, New York: Dr. Smith was good enough to send me a copy of his presentation, and I was very gratified to see that, as so often, the differences which seemed to exist between us were almost completely ironed out when he really had a chance to express himself as thoroughly as he has done in this paper. I think there is but little of what he has said in this very well constructed and very conservative presentation with which I cannot agree in principle. If there is any difference at all between us, it is only one of accent, certainly not of fact, and not even of interpretation of fact. Perhaps we accent our inferences somewhat differently simply because he and I have different genetic constitutions, or perhaps it is because he sees one end of these problems and I see the other; I send these patients away, and he gets them. Any such differences in actual conditions would account for the differences in our outlook upon the facts which he has presented.

I think that in some of these cases the emotional and stress factors may be stronger and in others less strong, and that the question here is really one of a difficult statistical, quantitative evaluation. My own observations have been such as to make me incline to pay more attention to the other factors rather than to the emotional and psychiatric ones. I know many cases. I recall many patients who have fared poorly when they were transferred from New York City to one type of climate and have fared well when they moved to another type of climate, although as far as could be ascertained the rest and relaxation in the place in which they fared poorly were the equivalent of those in the place in which they fared well. Many (but by no means all) patients fare poorly in high heat and humidity and well in dry warm climates. Many of my patients carry their troubles with them wherever they go and still fare exceedingly well when they do carry these same troubles to the climatic environment which is good for them. They carry their wives, their mothers-in-law, their economic problems, their social maladjustments, and their psychic traumas and tensions and frustrations and aggressions and submissions and neuroses with them and still seem to fare well when they get into the different, favorable climate.

I am convinced that, just as Dr. Smith has emphasized, a great deal of this benefit may depend on the humidity and the effect which it has upon the evaporation of fluid from the surface of the skin and upon the alterations of the fluids in and upon the skin. It is not only the sweat but, as Dr. Franz Herrmann was recently able to show, also the sebum which is influenced by the environmental heat and humidity. Owing to the interrelations between watery material and fatty material upon the skin surface, the emulsification and flow of fats and lipids depend to a certain degree upon the sweat and other watery materials present.

One of my most compelling reasons for paying more attention to the physiologic and climatic effects of the environment than to mental and emotional influences is that the psychiatric and emotional approaches in my patients have been so uniformly disappointing. Psychiatric approaches have failed in every particular and in every instance to clarify these dermatologic cases in regard to etiology or etiologic mechanisms. Moreover, the psychiatric studies have failed to fulfill any of the accepted postulates for proof of causation. Psychic influences have in my experience never reproduced the disease *de novo* in any person by any method, and psychiatric therapeutic approaches have, under controlled conditions, failed to prevent the attacks in any one of my patients. They have failed to bring even substantial relief, not to mention cure.

I have seen many dermatologic patients go to many good psychiatrists of various schools, types, and kinds, from classic Freudian analysts all the way to hypnotists and electroshock therapists, and none of these approaches has in my experience been scientifically illuminating or therapeutically worth while. One big objection to these approaches is that the psychiatric approach has prevented some of these patients from accepting and receiving classic dermatologic treatment, which could so often have given them relief. They have been so "psychiatrized," so a priori saturated with the idea that the skin disease must come from their mind and nerves and emotions that they often refuse simple classic dermatologic therapy, which might be tantamount to a cure in these types of cases, which are so frequently self-limited in their course.

DR. WALTER C. LOBITZ JR., Hanover, N. H.: I should like to say a word about the sweat retention phenomenon in the person with atopic dermatitis. I hoped that Dr. Sulzberger would bring up this point because we have discussed it together many times. Of course, sweat retention may occur secondary to any inflammatory dermatosis; atopic dermatitis is no exception. In our physiological studies on these people we are finding that the "atopic" will easily sweat

in the sites of predilection of his disease (antecubital, popliteal, face, neck areas, etc.) from emotional stimuli. Such emotional sweating, of course, produces the signs and symptoms of the sweat retention syndrome as easily as thermal sweating. A person may avoid thermal sweating by a change in environment, but he may take his emotional responses with him.

Perhaps this emotionally stimulated sweat retention phenomenon can explain the symptomatology of one of the psychosomatic components of this complex disease.

Dr. Clarence S. Livingood, Galveston, Texas: We are indebted to Dr. Smith and Dr. Garrett for this very interesting timely paper. I, too, practice dermatology in the state of Texas, but the climate in our part of the state is quite different from that of El Paso. Dr. Smith stated that the annual rainfall in the western part of the state may be as low as 8 or 9 in. (20 or 22 cm.) per year. In Galveston, we have had as much as 7 or 8 in. (17 or 20 cm.) of rainfall in one day, and with Houston we share the dubious distinction of having the highest humidity in the state. It is pertinent to add that Galveston is situated on a little island which is described by the Chamber of Commerce as a "semi-tropical Paradise" and as the "Playground of the Southwest," and by Lait and Mortimer, who wrote "U. S. A. Confidential," as "America's liveliest and least inhibited city."

I do not propose to compare the effects of climatic and other factors peculiar to the Gulf Coast of Texas on the course of atopic dermatitis with the effects of climatic factors which prevail in El Paso. However, it is appropriate to record that it is our impression that some patients from the western part of Texas who have atopic dermatitis and who elect to come to Galveston for treatment improve rather dramatically in our hot humid climate. On the other hand, some of our patients who live on the island of Galveston improve when they move to the western part of Texas. Many patients with this syndrome do not improve either in the western or the Gulf Coast section of the state.

I have been impressed by the fact that many of our patients with atopic dermatitis, and this includes infants, seem to have exacerbations when we have a so-called "Norther." This sequence of events results in a significant decrease of temperature, which persists for a variable period of time, and it means that the prevailing winds are from the north, that is, from Houston, rather than from the Gulf of Mexico, which bounds our city to the south. I do not think that these people have a conditioned reflex, but, rather, it seems probable that these exacerbations which follow a significant change in prevailing winds depend on increased exposure to various inhalants rather than on a change in temperature and humidity.

Finally, I cannot agree with Dr. Sulzberger in regard to the complete failure of psychiatric treatment in the management of some of these patients with atopic dermatitis. In my experience, prolonged psychotherapy has been helpful in certain cases, and, indeed, at the present time, I have two patients under my care who seem to have derived more consistent improvement with appropriate prolonged psychiatric therapy than from all other therapeutic measures which had been used previously. Nevertheless, I do agree with him that the diagnostic term "disseminated neurodermatitis" is an unfortunate one, and I believe that it should be discarded.

Dr. Arthur G. Schoch, Dallas, Texas: It occurs to me that one very obvious practical mechanical device should at least be mentioned in this discussion. I refer to refrigerated air conditioning in the homes of these patients. I am completely convinced that when these patients live in adequately air-conditioned houses they are not only more comfortable but that they also show objective improvement.

Dr. Leslie M. Smith, El Paso, Texas: I am very grateful to Dr. Lane, Dr. Sulzberger, and the others for their valuable discussions. There are many factors involved in this group of dermatoses, and their discussion should be a valuable part of the presentation. In stating that seborrheic dermatitis was sometimes the trigger mechanism which set off a generalized neurodermatitis, I meant such a condition as distinct from a generalized seborrheic dermatitis.

The stress factor varies in different persons. Some of these patients seem fairly stable, but many of those who seem so will later show signs of instability as we become better acquainted with them, and they often reveal sources of strain which the first history did not bring out.

The rapid evaporation of sweat from the skin, which occurs in a dry climate, is a source of relief to persons who have been experiencing considerable sweat on the skin surface. However,

some patients fare as well in Florida as they do in the Southwest. This probably depends partly upon how completely they are getting away from their business and domestic sources of tension, and partly upon the time of year. It is conceivable that a patient might fare well in Florida in the winter and not so well when the weather is hot and humid. It is a common experience that these patients improve most rapidly in the Southwest when the weather is neither cold nor windy, and the usual dry hot summer of the Southwest does not seem to bother them.

We do not think it necessary to send most of these patients to a psychiatrist, but those with marked emotional upsets often profit by such consultation. The average patient apparently does not.

I did not mean to imply that there are not allergic factors in some of these cases, but they have usually seemed of minor importance.

The possible effect of air conditioning on these cases is interesting. Perhaps living in a pleasant, dehumidified air, from which air-borne allergens are removed, would be of value in treating some patients, or even in preventing the development of their disease.

EPIDEMIC FAVUS OF THE GLABROUS SKIN

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JAMAICA, N. Y.

FAVUS is considered a rare mycotic disease in the United States. From time to time reports appear of endemic foci in various parts of the country,[1] usually in small numbers and in isolated rural communities where the personal hygiene of the involved patients is rather poor. In these endemic foci, the disease manifests itself primarily as an infection of the scalp, and the hairs become directly involved. Occasionally there is involvement of a nail or two. Sometimes the glabrous skin adjacent to the scalp becomes involved by a direct extension of the process out of the scalp.

This report is of an epidemic produced by Trichophyton schoenleini. It occurred entirely on the glabrous skin and was limited to the personnel of a large city hospital in New York.[2] In all, 22 persons were involved, and the majority were members of the nursing staff.

The first case (Table, E. K.) was seen on April 9, 1952. Miss E. K. a white student nurse, aged 20, visited the dermatology clinic complaining of a lesion on the left leg of about two weeks' duration. At the middle of the left leg anteriorly a half-dollar-sized erythematous ring was found, consisting of scaling papulovesicles. Inside the ring there were 8 or 10 tiny papules capped by yellow crusts, which, on close scrutiny, were cup-shaped and were typical scutula (Fig. 1).

Direct examination of the scutulum in 10% potassium hydroxide revealed a solid mass of fungus elements consisting largely of spores at the center and radiating filaments at the edges (Fig. 2).

Culture on Sabouraud's medium grew very slowly, with a luxuriant flower-like deep growth and a cerebriform rather waxy light to dark-brown surface growth (Fig. 3). Cracking of the medium occurred in typical fashion. Culture mounts revealed mycelia, chlamydospores, and many excellent examples of favic chandeliers (Fig. 4).

Discovery of this first case led to a screening survey of the student nurses, at which time 10 additional cases were discovered, and, in addition, a registered nurse, a practical nurse, and an orderly were also found to be infected. Approxi-

From the Department of Dermatology, Queens General Hospital, Queens, N. Y., Ida J. Mintzer, M.D., Director.

1. Barrett, C. C.: Endemic Favus, South M. J. **43**:685-689 (Aug.) 1950. Dobes, W. L.: Favus: Occurrence in Georgia: Report of 10 Cases, Urol. & Cutan. Rev. **52**:729-734 (Dec.) 1948. Robbins, S. J.: Favus in a Rural Community of New York, Arch. Dermat. & Syph. **58**:180-183 (Aug.) 1948. Eppright, B. R., and McCuistion, C. H.: Endemic Favus in Texas, ibid. **60**:1208-1209 (Dec.) 1949.

2. Queens General Hospital, Queens, N. Y.

Case Distribution of Epidemic Favus

Name	Ward	Date Discovered	Probable Contact	Nurse's Home Room	Location of Lesions	Age	Sex	Race	Description of Lesions	Micro	Culture
M. B.	7S	3/17/52	Original source (?)	311	Neck	18	F	W	Circinate lesion	Neg.*	Neg.
C. C.	7S	3/19/52	Original source (?) Gowns (?)	312	L. arm	19	F	W	Circinate with central scutula	Pos.	T. schoenleini
E. K.	8C	4/ 9/52	Gowns	507	L. leg	20	F	W	Circinate with central scutula	Pos.	T. schoenleini
M. T.	7S	4/20/52	Gowns	...	R. forearm	20	F	W	Circinate with central scutula	Neg.	Neg.
M. B.	7S	4/20/52	Gowns	314	L. arm L. forearm	19	F	W	Circinate with central scutula	Pos.	T. schoenleini
P. C.	8S	4/20/52	Patient 9 or gowns	503	Back	19	F	W	Circinate with central scutula	Neg.	Neg.
H. M.	7N	4/20/52	Gowns	521	R. arm	19	F	W	Circinate with central scutula	Pos.	T. schoenleini
C. M.	7S	4/20/52	Gowns	611	L. arm	19	F	N	Round plaque	Neg.	T. schoenleini
J. Mc.	8C	4/20/52	Gowns	517	L. arm	20	F	W	Circinate with central scutula	Pos.	Neg.
R. G. (Pract. Nurse)	7S	4/20/52	Gowns	...	L. forearm	38	F	W	Grouped scutula	Pos.	Neg.
Mrs. B. (Orderly)	7N	4/20/52	Gowns	...	L. arm	40	F	N	Round plaque	Neg.	Neg.
Miss C. (R. N.)	7N	4/21/52	Gowns	....	Neck	22	F	W	Circinate lesion	Neg.	Neg.
C. H.	8S	4/22/52	Gowns	...	L. leg	20	F	W	Circinate with central scutula	Pos.	T. schoenleini
M. T.	7N	4/28/52	Gowns and girdle	508	R. leg and thigh, L. thigh	19	F	W	Circinate with central scutula	Pos.	T. schoenleini
B. J.	7N	4/28/52	Gowns	508	L. leg (2), r. knee, shoulder	20	F	W	Round plaques	Neg.	Neg.
C. N.	7N	4/28/52	Gowns	512	L. leg	20	F	W	Grouped scutula	Neg.	Neg.
D. M.	7S	4/29/52	Gowns	...	Neck	23	F	W	Circinate lesion	Pos.	T. schoenleini
(R. N.) K. P.	7N	5/ 5/52	Gowns	302	Neck	19	F	W	Round plaque	Pos.	T. schoenleini
B. J.	(Porter, nurses' quarters)	5/ 6/52	Discarded dressings	...	L. forearm	69	M	W	Round plaque	Pos.	T. schoenleini
M. C.	7N	5/12/52	Gowns	518	R. leg	21	F	W	Grouped scutula	Pos.	Neg.
M. W.	(Housekeeper, nurses' quarters)	5/27/52	Patients 10 and 11, nurses' bedclothes	...	R. leg	68	F	W	Round plaque	Pos.	T. schoenleini
P. T.	8C	6/10/52	Gowns	531	L. leg	19	F	W	Circinate with central scutula	Pos.	Neg.

* In most of the cases in which there were negative mycological results the patients had had previous self-therapy.

Fig. 1.—Ringed clinical lesion showing scutula and tinea-circinata-like appearance.

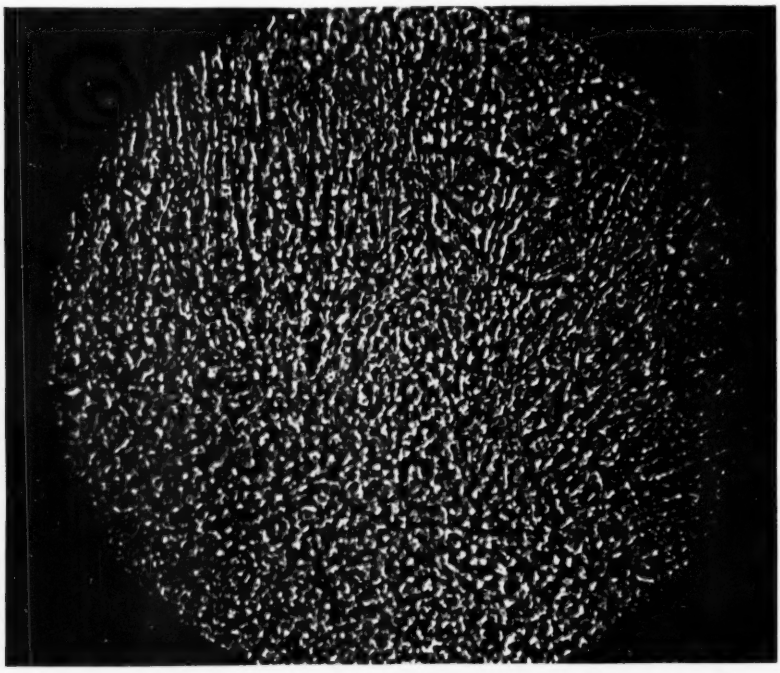

Fig. 2.—Photomicrograph of the edge of a scutulum mounted in 10% potassium hydroxide showing innumerable radiating mycelia from the central mass of fungus elements.

mately a week later three student nurses and a registered nurse were added to this series of cases. The following week another student nurse and a male porter at the nurses' quarters were found to be infected. The succeeding month infection was discovered in two additional student nurses and in a female housekeeper at the nurses' quarters. In all, 16 student nurses, 2 registered nurses, 1 practical nurse, 1 female ward orderly, a porter, and a housekeeper at the nurses' quarters were infected in this epidemic—a total of 22 cases (Table).

It will be noted that all but one of these persons were females.

The lesion described in the first case was the most characteristic and the one most commonly seen. However, other types of reaction were also found. The infec-

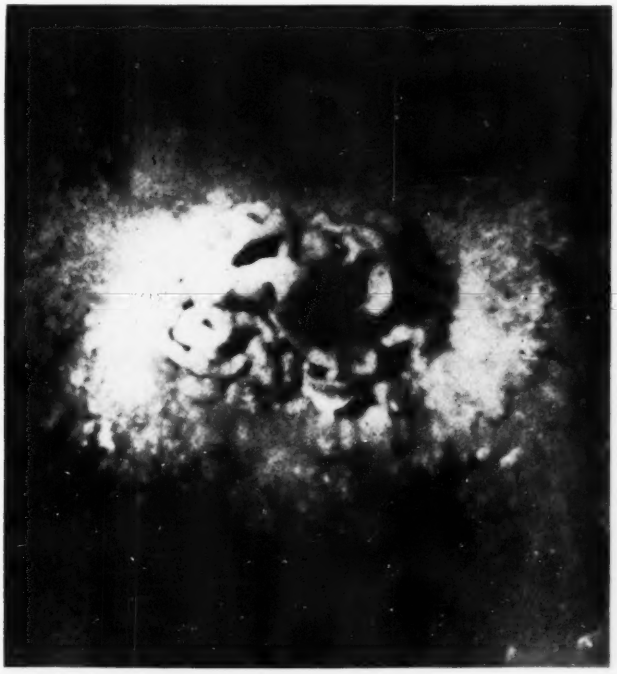

Fig. 3.—T. schoenleini in culture as grown in Sabouraud's dextrose agar medium. Note cerebriform surface and luxurious subsurface growth.

tion in three cases manifested itself as a ringed lesion, with a scaly papulovesicular border and a clear center, which without a culture could not have been differentiated from any other ringworm lesion. Six persons manifested erythematous round slightly scaly plaques. Three lesions consisted of only a cluster of follicular papules, capped by scutula.

All the lesions were found on the glabrous skin, occurring in almost every case on the extremities or the neck. No involved hairs were found. The only hairs in the vicinity of the lesions were lanugo in type, and none of these hairs were found to be infected. There were no scalp lesions in this series.

Three patients had more than one lesion. One patient had four lesions. Two student nurses had two lesions each, and in one of these a third lesion developed 36 days after her first lesions were discovered.

On investigating the source and spread of this epidemic, it was learned that two affiliated student nurses from another nursing school in another city in upstate New York had lesions before arriving at our hospital.[3] These girls, at the time of the onset of this epidemic, were assigned to the pediatric wards. A review of the Table will reveal that all the hospital personnel involved were working on either the sev-

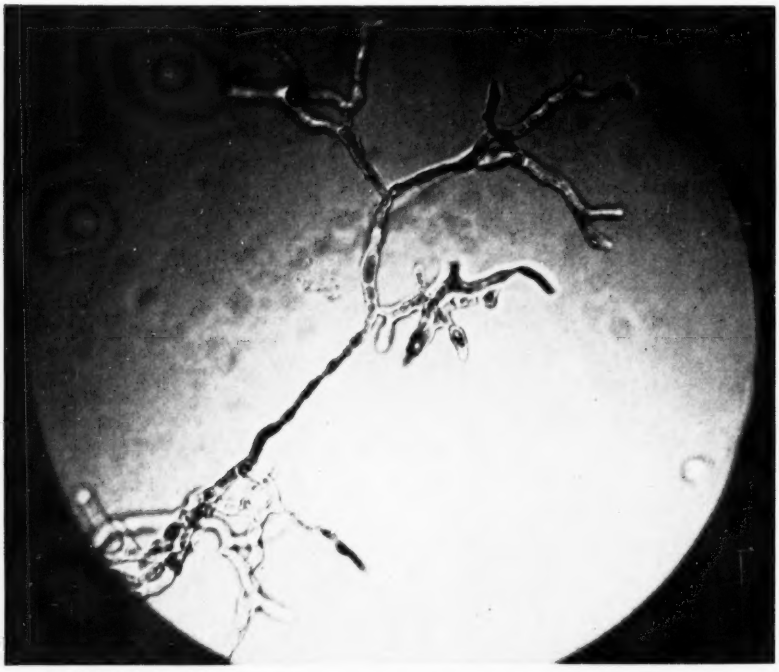

Fig. 4.—Culture mount. Photomicrograph revealing characteristic chandeliers.

enth (Pediatrics) or the eighth (Nursery or Obstetrics) floors of the hospital. Since none of the hospital patients were infected and since all but a few of the lesions occurred on the neck, the midportion of the legs, or the upper extremities, I feel that the primary mode of transmission of the infection was the hospital gowns. As a nurse enters a cubicle to care for a patient, she puts on the gown which hangs at its entrance. In spite of the fact that these gowns were changed daily, during the course of a single day the same gown was worn by several nurses. In the case of the student in whom a new lesion developed 36 days after her original lesions were diagnosed, one of her original lesions was on the upper anterior right

3. Communication with the home school did not confirm the source of the infection, since they had no knoweldge of any such cases either among the student nurses or among any of the hospital patients.

thigh, at a point where the edge of her girdle passed across the lesion. Since her girdle was reversible, she inadvertently wore the garment, on at least one occasion, reversed, so that the contaminated area contacted the same area of her opposite thigh, and it was at this point that her new lesion appeared.

The porter, and the only male patient in this series, emptied the trash baskets into which the student nurses discarded the dressings which were worn over their lesions, in an effort to prevent further spread of the disease. His lesion appeared on the forearm, which was obviously exposed.

The housekeeper who was infected had many contacts with the students, their clothes, and their bedclothes, and especially with the patients who had four and three lesions respectively and who were roommates. (None of the other patients were roommates.)

Immediately prior to this epidemic another patient, with no apparent contact or relationship to any of the other patients, was seen in the clinic, and a diagnosis of tinea circinata was made. Cultures, however, grew T. schoenleini.

As regards therapy, all these infections responded fairly readily to topically applied fungicides. The average time required for a cure was two to three weeks. Among the fungicides used were 5% ammoniated mercury ointment, half-strength benzoic and salicylic ointment (Whitfield's Ointment), zinc undecylenate ointment (Desenex), Asterol (2-dimethylamino-6-[β-diethylaminoethoxy]-benzothiazole) dihydrochloride ointment and powder, and 2% methylrosaniline chloride (gentian violet) solution. The methylrosaniline chloride was completely ineffective. The Asterol proved to be the most effective.

No further cases have been discovered in over six months. It must, therefore, be assumed that no further infections will apear in this small and very localized epidemic.

This epidemic, in addition to its unusual qualities, should suggest the importance of routine microscopic and cultural studies of all mycotic infections seen by the dermatologist. It should also make one ever alert to the fact that fungi, uncommon in this country at present, seem to be infiltrating and establishing themselves and thus creating new problems in diagnosis and therapy.

SUMMARY

An epidemic of favus of the glabrous skin produced by infection with T. schoenleini is reported. All the cases occurred among the personnel of one large city hospital. No scalp infections were found.

88-56 163rd. St.

Ida J. Mintzer, M.D., assisted in the handling of this epidemic. Emanuel Muskatblit, M.D., examined the cultures and microscopic preparations and confirmed the identification of the causative organism, Trichophyton schoenleini. Mrs. M. Pikuritz, photographer, Queens General Hospital, prepared the photographs for this paper.

OCULAR PSORIASIS

Clinical Review of Eleven Cases and Some Comments on Treatment

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PSORIASIS is one of the diseases encountered frequently in the practice of the dermatologist. In the textbooks of dermatology all possible locations and involvements of psoriasis are discussed in detail, except one: psoriasis affecting the eye. Why the dermatologist, who is interested in eye manifestations of syphilis, rosacea, pemphigus, and other diseases, should not be interested in psoriasis of the eye, poses an unanswered question. Is ocular psoriasis so rare or unimportant, or should the diagnosis of this condition be left entirely to the ophthalmologist? Is the ophthalmologist sufficiently aware of the possibility of psoriasis to diagnose it correctly?

In the ophthalmological field de Schweinitz,[1] in his textbooks, mentioned a number of dermatological conditions affecting the eye, but fails to list psoriasis. Fuchs [2] states:

In the case of *other exanthemata*, too, for instance in macular and papular syphilides, in pityriasis, psoriasis, ichthyosis, herpes iris, dematitis herpetiformis, lepra, etc., the conjunctiva is sometimes characteristically implicated.

He does not describe the nature of psoriatic implication of the eye and does not mention the cornea as a possible site of involvement. L. W. Fox [3] states:

Psoriasis is a very rare condition of the skin of the eye lids, characterized by hyperemic patches, by imbricated mother-of-pearl scabs. The removal of the scales reveals a superficial inflammation of the skin. Psoriasis of the face is always an accompaniment.

This author also does not consider the cornea as a location for psoriatic changes.

The best account of the subject is given by W. Stewart Duke-Elder [4]

Psoriasis occasionally gives rise to ocular symptoms of considerable severity, which differ considerably from case to case, and have a strong tendency to appear and disappear with the cutaneous eruption. A nonspecific chronic conjunctivitis, sometimes with a considerable amount of secretion, is relatively common. It is more rare for plaques on the lid to spread over on

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1. de Schweinitz, G. E.: Diseases of the Eye, Ed. 10, Philadelphia, W. B. Saunders Company, 1924.

2. Fuchs, E.: Textbook of Ophthalmology, Philadelphia, J. B. Lippincott Company, 1899.

3. Fox, L. W.: Diseases of the Eye, New York, Appleton-Century-Crofts Company, Inc., 1907.

4. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, C. V. Mosby Company, 1944. Vol. 2.

to the conjunctiva than to appear upon it separately. Healing may involve Xerosis, Symblepharon and Trichiasis. A further rare complication is an involvement of the cornea. The typical lesion shows a triple distribution, comprising a thickening of the epithelium with erosions, an infiltrated zone under Bowman's membrane with superficial vascularization and a homogenous opacity in the deep stroma. Several efflorescences of this nature may appear, more frequently limbal than central and usually bilateral without much accompanying irritation. Slow chronic ulcers may develop, which may result in phtysis bulbi. An iritis has been reported (Morax 1893). Treatment should be confined to that of the general condition, for Chrysarobin is dangerous to use near the eye.

Toth [5] reports one scaly lesion on one upper eyelid in a male patient and concludes, "on the elbows and on the scalp there were also scaly conglomerations. They were diagnosed by a dermatologist as psoriasis, therefore the changes in the eyelid were consistent with psoriasis."

I have reviewed 90 unselected cases of psoriasis seen in my office between 1944 and 1952. The diagnosis in all the cases was made on clinical grounds only, without the help of biopsy or other laboratory tests, except for blood serology in some cases. All the patients showed the clinical characteristics of the psoriatic lesions, the typical distribution, family history, recurrent attacks, etc. Ocular involvement was found in 11 cases out of 90. There were 42 male patients and 48 female patients.

The following are brief reports of the 11 cases of psoriasis of the eye.

REPORT OF CASES

Case 1.—Leo P., a 31-year-old white man of French extraction, had been suffering from red eyelids for several years. Lately, he was seen by two eye specialists, who diagnosed that he was suffering from an "allergy of some kind." He was treated with sulfathiazole ointment, and there was temporary improvement. Several months ago he noticed two round scaly patches in the scalp.

Examination revealed the following findings: The edges of both eyelids were swollen and red, with the erythema reaching into the skin of the eyelids. In the scalp, about an inch (3 cm.) from the hairline to the right from the midline there were two round elevated erythematous patches the size of a quarter and a half dollar. The patches were covered with white scales, which, on removal, left bleeding points.

If the typical psoriatic lesions in the scalp, only a few inches away from the eye, had been noticed by the ophthalmologist, he could have made the correct diagnosis.

Case 2.—Anna Q., a 48-year-old white woman of Irish parentage, gave a history of an infection on both eyes occurring off and on for about a year. She was treated with sulfathiazole ointment by an ophthalmologist. About three weeks before she was seen by me, a rash suddenly developed all over the body.

Examination revealed the following findings: There were bilateral conjunctivitis and blepharitis. There were generalized papular eruptions on the skin. The lesions consisted of drop-like scaly papules, exhibiting bleeding points after removal of scales. The blood Wassermann test gave a negative result. A diagnosis of psoriasis guttata was made.

This case started out with eye symptoms. The generalized eruption may have been precipitated by sensitivity to the sulfa drug.

Case 3.—Arthur R., a 44-year-old white man of Scottish descent, was first seen in 1946. He had been suffering from reddish scaly patches in the groin and on the penis for about one year. Examination showed reddish scaly confluent patches in the groins and on the glans penis. The edges of the eyelids were thickened and erythematous, and there was bilateral conjunctivitis. A diagnosis of psoriasis and psoriatic blepharoconjunctivitis was made. This patient improved with conventional treatment, but he had a recurrence of the eye symptoms two years later.

5. Toth, Z.: Psoriasisefflorescenz am Lidrand, Klin. Monatsbl. Augenh. **114**:562, 1949.

Case 4.—John R., a 72-year-old white man of Scottish parentage, father of Arthur R. (Case 3), complained of itchy sores on both eyes of about three months' duration. Both upper eyelids showed thickening and redness on the edges. Occasional scales and specks of exudate were visible. Because of the duration and symmetry of the lesions and the familial history, a diagnosis of ocular psoriasis was made.

This patient showed ocular psoriasis alone, while his son (Case 3) was suffering from generalized psoriasis with eye involvement.

Case 5.—Walter W., a 68-year-old white man of English descent, complained of a reddish scaly patch in the scalp of seven months' duration. The lesion presented a slightly elevated reddish round plaque covered with white scales, measuring about 6 cm. in diameter. There were also scaly patches in the external ear canals. A diagnosis of psoriasis was made. After three months of weekly or bimonthly treatment epiphora and photophobia suddenly developed in the left eye. There was injection of the conjunctiva in the lateral part of the upper eyelid and eyeball. The lid was edematous, and there was a large patch of reddish velvet-like granulation in the mucous membrane. There were also two small granulomatous patches in the conjunctiva of

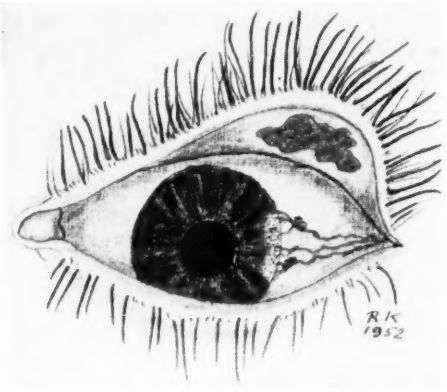

Fig. 1 (Case 5).—Psoriatic conjunctivitis and keratitis.

the eyeball close to the limbus corneae, located at about 3 o'clock. Concomitant injecting blood vessels were reaching through the granulations into the cornea and ending in a small area of opacity inside the cornea close to the limbus. The eye condition cleared within 10 days under medication with yellow mercuric oxide.

In this patient with a common form of psoriasis psoriatic conjunctivitis and keratitis developed temporarily.

Case 6.—Francis R., an 11-year-old boy of Irish parentage, in good general health, complained of redness and swelling on the edges of the upper eyelids which had been present for about one month. During the last two weeks the eyelashes in the middle part of the upper lids were falling out, and the lids were stuck together in the morning. One sister, aged 20, had similar eye trouble, and his mother and another sister, Elizabeth, aged 23, had had the same affliction in the past. One grandfather, on the mother's side, also had the same kind of eye trouble. His 23-year-old sister had been treated by me two years previously for psoriasis. She was suffering from scaly patches in the scalp and in the external ear canals, and she had dotted fingernails.

Examination revealed the following findings: The margins of both upper lids showed redness, thickening, and scaling. Some scales were adherent to the eyelashes. The middle parts of the lids were bare of eyelashes. There was itching, photophobia, and injection of the conjunctivae. There were no lesions elsewhere on the body. The diagnosis of psoriasis of the eyelids was made

on the basis of the scaly appearance of the lesions and the history of psoriasis, ocular and generalized, in several members of the family.

Case 7.—Patricia R., an 18-year-old high school girl of Irish parentage, complained of scaly patches on the elbows, knees, and scalp. The findings were consistent with typical psoriasis. She was treated in November and December, 1948, and again in March, 1949. In April, a new spot was noticed on the scalp, and a week later a small reddish scaly spot appeared on the edge of the left upper eyelid. The lesion caused no complaint and no disability and disappeared without treatment.

This was a case of generalized psoriasis, with temporary involvement of one eyelid.

Case 8.—Chester W., a 66-year-old white man of English descent, complained of red scaly patches on the scalp and about the ears and eyes. He also had several patches on both legs, below the knee. The duration was several months. The clinical appearance of the lesions was typical of psoriasis. He was treated with a salve by another physician and redness, itching, and weeping around the left eye developed during the last two weeks. The left eye and the conjunctiva remained normal. A diagnosis of psoriasis and dermatitis venenata was made. During four weeks of conventional treatment, the patient had improved considerably. No topical application was used near the eyes, except boric acid compresses. One morning the patient woke up with itching and swelling in the left eye. Examination showed conjunctivitis, epiphora, and photo-

Fig. 2 (Case 11).—Psoriatic blepharitis.

phobia. The condition cleared rapidly with the use of yellow mercuric oxide ointment. This was a typical case of generalized psoriasis, with development of psoriatic conjunctivitis during treatment.

Case 9.—Fernande D., a 36-year-old housewife of French extraction, gave a history of having had psoriasis for years. The condition started with scaly patches in the scalp, and a diagnosis of psoriasis was made by several physicians. The condition had healed and reappeared several times. At present the scalp is normal. For the last year her eyes have been red and itchy.

Examination revealed the following findings: Both upper and lower lids showed swelling and redness on the edges. There was an occasional scale at the base of some of the eyelashes. Two-thirds of the eyelashes were missing. The patient had photophobia and epiphora.

This was a long-standing case of psoriasis in which psoriatic blepharoconjunctivitis developed at a time when no other involvement was present.

Case 10.—Willard H., a 58-year-old white truck driver of English descent, had never had skin trouble before. Three weeks before he noticed spots on the legs and trunk, and later a rash broke out all over the body. Examination showed a generalized small papular scaly rash, with most intense involvement on the extensor sides. Blood Hinton test gave a negative result. Clinically the findings were consistent with psoriasis guttata. He received treatment with ultraviolet rays and coal tar and improved gradually for six consecutive weeks. No medication was used on the face, and the eyes were properly shielded during treatment. On the seventh

visit he complained of itching and redness in both eyes. There was conjunctivitis, with photophobia and epiphora. On the left eye there was a horizontal band of enlarged arterioles visible, leading from the outer angle on to the limbus corneae. At about 3 o'clock there was no visible change in the cornea.

This was a first attack of generalized psoriasis, with development of psoriatic conjunctivitis during treatment.

CASE 11.—Cyril A., a 42-year-old white man, a switchboard operator of Scottish parentage, gave a history of having had a few scaly spots for the last seven years. One sister, aged 55, had had sore eyes for several years and was treated by an ophthalmologist for ulcers on the eyelids. Examination showed small elevated scaly papules on the left ear and on the dorsum of the left hand, a larger scaly plaque on the glans penis, and a scaly papule on the edge of the lower eyelid. This lesion on the eyelid measured 3 mm. in diameter and was located in the middle of the eyelid. Deep erythema extended from the lesion about 2 mm. into the surrounding skin. There was great paucity of eyelashes on the lower lids, and they were almost missing on the affected lid. The history and findings were consistent with psoriasis.

This was a case of dermal and ocular psoriasis; one sibling also suffered from ocular psoriasis.

COMMENT ON TREATMENT

In most cases the use of 0.5 to 1.0% of yellow mercuric oxide ophthalmic ointment will suffice. Sanford R. Gifford uses x-rays on the eyelids (95 to 100 kv., 3 ma., 100 r, weekly for two or three treatments) in cases of long standing. Although the structures of the eyes are considered only slightly sensitive to γ radiation, this type of treatment is not attractive because of its possible legal implications, years after treatment. I have found that a square half-strength 5 mg. radium plaque used in doses of ½ to 1 minute applied without filtration to the lids at weekly intervals will yield sufficient β and γ radiation without endangering the underlying structures of the eye. One eyelid can be covered with two applications of the plaque. While the right hand of the operator holds the plaque by means of a handle flat to the surface of the lid, the left hand pulls the lid away from the eye. The upper lid will be pulled upwards and the lower lid will be pulled downwards while the patient is asked to look into the opposite direction. Thus, there is always an air space of 1 to 2 mm. between the eyeball and the inner surface of the lid. Usually two to four such treatments will clear a case of long-standing blepharoconjunctivitis when yellow mercuric oxide treatment alone has not succeeded.

SUMMARY

The clinical features of 11 cases of ocular psoriasis are reported briefly. In these cases four patients, Cases 5, 7, 8, and 10, showed dermal psoriasis, gradually clearing under treatment, with sudden development of a short-lived ocular attack before recovery. In only one of these four patients did keratitis develop. In this patient also the keratitis cleared promptly without permanent damage. Three patients, Cases 1, 3, and 11 showed dermal and ocular psoriasis at the same time. One patient, Case 2, started out with only ocular psoriasis and generalized psoriasis developed explosively during treatment with a sulfa drug. Only two patients showed ocular psoriasis alone, one of them (Case 9) had a history of long-standing dermal psoriasis, while another patient (Case 6) showed ocular psoriasis alone, but had a history of several members of his family having suffered from dermal and ocular psoriasis.

Conjunctivitis or blepharitis occurring during treatment of psoriasis might be considered merely coincidental; however, I did not observe this occurrence in other dermatoses, except in an occasional case of pemphigus or rosacea. Contrary to the opinion of W. Stewart Duke-Elder, ocular psoriasis alone does occur. It is this type of psoriasis which masquerades under the disguise of chronic conjunctivitis, infection, allergy of some kind, etc. The correct diagnosis of the condition is of importance because it can save the patient from harm by the unwarranted use of sensitizing drugs and because it will save expense in avoiding a futile hunt for a phantom allergy. Judging from the small number of cases, in one out of nine cases of psoriasis ocular symptoms will develop. This is a relatively high incidence and merits more attention in the textbooks of dermatology than it has received up to now. Ocular psoriasis in the male seems to occur more than twice as frequently as in the female.

EOSINOPHILIC RESPONSE AFTER INUNCTION OF HYDROCORTISONE OINTMENT

Experiments Demonstrating Lack of Significant Absorption and of Systemic Effects

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RECENTLY the local application of hydrocortisone acetate ointment has been reported to have a favorable effect in a number of dermatoses.[1] Because of this the possible percutaneous absorption of hydrocortisone and potential systemic effects were thought worthy of investigation. One of the reasons which had been considered as a hypothetical explanation of the effectiveness of topically applied hydrocortisone in contrast to the ineffectiveness of topically applied cortisone was the possible percutaneous absorption of the former.[2] The previously demonstrated apparent lack of absorption of topically applied cortisone in normal subjects fits in with this theory.[3] It was also theorized that the apparent beneficial effects of hydrocortisone acetate ointment upon skin lesions located beyond and removed from the actual site of application could possibly be explained on the basis of absorption, with mild systemic effects.

It is today well established that a reduction in the circulating eosinophile count almost regularly follows the oral administration or injection of cortisone and hydrocortisone.[4] For this reason we chose this count as a test for absorption or nonabsorption of the topically applied hydrocortisone, just as Danto and Maddin [3] had done in their studies of cortisone ointment.

This study was aided by a grant from Merck & Company, Inc., Rahway, N. J.

From the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School (Dr. Marion B. Sulzberger, Chairman), and the Service of Dermatology and Syphilology of Bellevue Hospital (Dr. Frank C. Combes, Chief of Service).

1. Sulzberger, M. B., and Witten, V. H.: The Effect of Topically Applied Compound F in Selected Dermatoses, J. Invest. Dermat. **19**:101, 1952. Sulzberger, M. B.; Witten, V. H., and Smith, C. C.: Hydrocortisone (Compound F) Acetate Ointment in Dermatological Therapy, J. A. M. A. **151**:468, 1953.

2. Goldman, L.; Thompson, R. G., and Trice, E. R.: Cortisone Acetate in Skin Disease: Local Effect in the Skin from Topical Application and Local Injection, A. M. A. Arch. Dermat. & Syph. **65**:177, 1952. Sulzberger, M. B.: Some Aspects of ACTH and Cortisone in Dermatology, Tenth International Congress of Dermatology, London, July, 1952, Excerpta Med. XIII Dermatology & Venereology **6**:364, 1952.

3. Danto, J. L., and Maddin, S.: The Eosinophilic Response in Normal Subjects Following the Inunction of Cortisone Ointment, J. Invest. Dermat. **18**:381, 1952.

4. Thorn, G. W., and others: Studies on the Relation of Pituitary-Adrenal Function to Rheumatic Disease, New England J. Med. **1241**:529, 1941. Nelson, D. H.; Sandberg, A. A.; Palmer, J. G., and Tyler, F. H.: Blood Levels of 17-Hydroxycorticosteroids Following the Administration of Adrenal Steroids and Their Relation to Levels of Circulating Leukocytes, J. Clin. Invest. **31**:843, 1952.

METHOD

The method used by Danto and Maddin in studying the absorption of cortisone ointment was also employed in this study, with but few modifications. A special Levy counting chamber with the Fuchs-Rosenthal ruling was used for performing the circulating eosinophile counts.

Eight normal adult volunteers were studied in this experiment. Six grams of an ointment [5] containing 25 mg. of hydrocortisone acetate per gram of base were employed for each inunction. (The ointment base consists of zinc stearate, propylene glycol, polyethylene glycol [carbowaxes], and water.) Each person rubbed in the ointment for approximately 10 minutes to the back, upper arms, and legs. A base line circulating eosinophile count was done the day prior to the inunction at 2 p. m. and 4 p. m. The application of the ointment took place at 10 a. m. Circulating eosinophile counts were done again 4 hours after the inunction (2 p. m.), and repeated at 6 hours (4 p. m.) and 28 hours (2 p. m.).

TABLE 1.—*Eosinophile Response in Normal Persons Following the Inunction of Hydrocortisone Acetate Ointment as Compared with the Inunction of the Ointment Base Alone*

		Time Blood Taken							
		Base Line Counts (Before Inunction)		Counts After Inunction			Rise or Fall in Count as Compared with Base Line Counts		
				2 P.M.	4 P.M.	2 P.M.			
				Hours After Inunction					
Case	Ointment	2 P.M.	4 P.M.	4	6	28	4 Hr.	6 Hr.	28 Hr.
1	C *	275	300	225	209	287	F ‡	F	R §
	H †	259	84	259	278	194	U ‖	R	F
2	C	144	119	94	100	100	F	F	F
	H	75	88	106	109	47	R	R	F
3	C	58	81	94	100	104	R	R	R
	H	50	35	109	125	141	R	R	R
4	C	163	138	213	81	142	R	F	F
	H	119	103	93	128	169	F	R	R
5	C	456	419	216	238	225	F	F	F
	H	256	234	234	225	256	F	F	U
6	C	25	38	31	19	31	R	F	R
	H	31	35	16	44	106	F	R	R
7	C	156	188	584	344	331	R	R	R
	H	588	369	428	575	344	F	R	F
8	C	147	156	25	78	25	F	F	F
	H	78	47	53	86	119	F	R	R

* C indicates ointment base (control).
† H indicates hydrocortisone acetate ointment.
‡ F indicates fall.
§ R indicates rise.
‖ U indicates unchanged.

A control study was done in the manner outlined above on the same eight persons after a two-week waiting period with the ointment base alone.

Seven patients with generalized skin disease were selected from the dermatology wards of Bellevue Hospital to see if any absorption could be demonstrated through diseased skin and skin in which the epidermis was not intact. The method outlined above was used, with the exception that only one base line count was done. In these patients the control study with the ointment base alone was done after a three-day waiting period.

RESULTS

As shown in Table 1 and Table 2 there was no consistent alteration in the circultating eosinophile count after the inunction of hydrocortisone acetate ointment as compared with the base line circulating eosinophile counts, either in normal persons or in hospitalized patients with generalized skin disease. Nor could any significant

5. Hydrocortone acetate ointment 2.5% was furnished by Merck & Company, Inc.

difference be demonstrated in the circulating eosinophile counts following the inunction of hydrocortisone acetate ointment as compared with inunction of the ointment base alone (control).

Table 1 shows the results of 24 circulating eosinophile counts at 4 hours, 6 hours, and 28 hours following the inunction of hydrocortisone acetate ointment on eight normal persons. It will be seen that 13 showed a rise in the eosinophile count; 9 a fall in the eosinophile count; and the count remained unchanged in 2. Also shown in Table 1 are 24 circulating eosinophile counts at 4 hours, 6 hours, and 28 hours following the inunction of the ointment base alone; here 10 showed a rise in the circulating eosinophile count, and 14 a fall in the circulating eosinophile count.

Table 2 shows the results of 21 circulating eosinophile counts at 4 hours, 6 hours, and 28 hours following the inunction of hydrocortisone acetate ointment on seven

TABLE 2.—*Eosinophile Response in Persons with Generalized Skin Disease Following the Inunction of Hydrocortisone Acetate Ointment as Compared with the Inunction of the Ointment Base Alone*

	Time Blood Taken								
	Base Line Counts (Before Inunction)		Ointment Base (Control)			Hydrocortisone Ointment			
			2 P.M.	4 P.M.	2 P.M.	2 P.M.	4 P.M.	2 P.M.	
			Hours After Inunction						
Case §	2 P.M.	4 P.M.	4	6	28	4	6	28	
1	272	288	125	93	83	138	269	156	
			F *	F	F	F	F	F	
2	16	19	13	25	22	19	100	100	
			F	R †	R	R	R	R	
3	19	118	19	44	22	6	81	106	
			U ‡	F	R	F	F	R	
4	35	19	156	13	12	19	50	109	
			R	F	F	F	R	R	
5	19	19	13	6	19	3	31	0	
			F	F	U	F	R	F	
6	44	56	44	50	63	37	44	69	
			U	F	R	F	F	R	
7	16	16	44	44	37	3	25	25	
			R	R	R	F	R	R	

* F indicates fall in circulating eosinophiles as compared with base line count.
† R indicates rise in circulating eosinophiles as compared with base line count.
‡ U indicates unchanged as compared to base line count.
§ Cases 1 and 2, atopic dermatitis; 3 and 6, pemphigus foliaceus; 4, bullous eruption ?; 5, generalized contact dermatitis; 7, psoriasis.

patients with generalized skin disease. In this group 10 showed a rise in the circulating eosinophile count, 8 a fall in the circulating eosinophile count, and in 3 the eosinophile count remained unchanged. Table 3 also shows the results of 21 circulating eosinophile counts at 4 hours, 6 hours, and 28 hours following the inunction of the ointment base alone on the same seven patients. Here 11 showed a fall in the circulating eosinophile count, and 10 showed a rise in the circulating eosinophile count.

SUMMARY AND INFERENCES

No significant change was demonstrated in the circulating eosinophile count when 6 gm. of ointment containing a total of 150 mg. of hydrocortisone acetate was rubbed into normal skin areas of human volunteers or into affected skin areas of patients with generalized skin disease. This indicates that there was either no absorption or, at any rate, insufficient absorption to produce a drop in the circulating eosinophile count.

It is of course possible that the test used as a criterion of absorption and systemic effects was not sufficiently sensitive to demonstrate blood changes which might result from the absorption of very minute amounts of hydrocortisone. It is however unlikely that the small amounts which would thus escape detection could account for the therapeutic effects reported.

The absence of experimental evidence of significant absorption on topical application is also in consonance with the previously reported complete absence of systemic ill effect from prolonged clinical use of hydrocortisone ointment in the treatment of selected skin diseases.

PROBLEMS OF MILITARY DERMATOLOGY

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IN PLANNING this presentation I have considered three basic factors: (1) the contributions made by dermatology and dermatologists that are of direct and indirect value to the Armed Forces, (2) the contributions that the Armed Forces and the office of the Secretary of Defense have made to dermatology, and (3) the answer to the question, "What further should be done to make dermatology, dermatologists, and the Armed Forces more mutually advantageous?"

Dermatology as a science and dermatologists individually have contributed much to various and broad aspects of military dermatology, especially when it is remembered that prior to World War II dermatology and dermatologists were not recognized as such by the Armed Forces. Throughout the first year of World War II it became clear that dermatologists were a necessity and that cutaneous diseases constituted one of the major causes of hospitalization and disability.

In 1944, the total number of physicians on active duty who were classed as dermatologists by the Army, Air Force, Navy, and United States Public Health Service was 490; 155 of them had been certified by the American Board of Dermatology and Syphilology. It should be noted that at the same time only 644 dermatologists had been granted certificates. Numerous other dermatologists at that time were eligible for board examinations. For the most part these men practiced dermatology in the services, although instances occurred in which a dermatologist performed no medical duties of any type for many months. This is a situation now supposedly remedied, but even at present some trained dermatologists are being used for purposes other than as specialists in dermatology.

One has only to review the contents of the ARCHIVES OF DERMATOLOGY AND SYPHILOGY and *The Journal of Investigative Dermatology* during the war years to realize what important advances in knowledge and therapy were being made in dermatology and how these advances aided the Armed Forces as they were developed and applied by dermatologists. Articles originated not only from the continental United States, but also from stations overseas; these articles described pure research as well as case reports and clinical investigation, and many of them were

From the Section of Dermatology and Syphilology, Mayo Clinic.

Read at the meeting of the American Academy of Dermatology and Syphilology, Chicago, Dec. 10, 1952.

Cooperation was obtained in the assembling of material from The Armed Forces Medical Policy Council under the chairmanship of Dr. Melvin A. Casberg, from Vice Admiral J. T. Boone, Chief Medical Director of the Veterans Administration, from Dr. Theodore J. Bauer, Medical Director and Chief, Division of Venereal Diseases, U.S.P.H.S., from Lieutenant Colonel William Piper, and from Captain Robert L. Gilman of the United States Navy.

of lasting importance. For example, one may cite studies of lichenoid eruption with or without anhidrosis from quinacrine hydrochloride (Atabrine dihydrochloride), fluorescence produced by quinacrine hydrochloride, the excellent work relating to miliaria, tropical anhidrotic asthenia, epidermolysis bullosa, cutaneous diphtheria, well-controlled studies of methods of therapy, including control of parasitic diseases, new types of contact dermatitis, studies of urticaria caused by heat, and the advances in treatment of syphilis and other venereal diseases. Also produced was a fine manual of dermatology by Pillsbury, Sulzberger, and Livingood.[1] A fair conclusion appears to be that dermatologists involved in World War II were alert, conscientious, and produced excellent work.

This was not all, however, nor was the work confined to the young or middle-aged dermatologist; I have in mind Dr. J. Gardner Hopkins who did magnificent work under trying conditions. It was my privilege to be near him and to see much of him in New Guinea, in 1944. Dr. Udo Wile, whose work in the field of syphilis is well known, also deserves mention.

Pillsbury and Livingood,[2] in 1947, reviewed their experiences and assessed the successes and failures that dermatology contributed to the over-all mission of prevention and cure of disease in the United States Army. This article reveals the sorry state of military dermatology at the beginning of the war, describes the improvement made, and suggests future courses to follow. To those interested, this article is required reading.

In spite of original shortcomings, the later inclusion of theater, Army and base consultants in dermatology, the designation of certain general hospitals in the Zone of the Interior as dermatologic centers, the increasing awareness of commanding officers of both hospital and tactical units of problems of military dermatology, and the development of new therapeutic techniques all led to a tremendous improvement in the standards of dermatologic care for those afflicted with cutaneous disease.

Since the official cessation of World War II, dermatologic interest and activity have continued. The concern of civilian dermatologists and their societies, the regard of the military dermatologists, and the enlightened "brass hats and VIPs," all point toward an improvement of dermatology as it exists in both civilian life and military situations, for these two facets cannot be separated widely. Following are a few examples of agencies and activities that indicate this continued trend (these will also indicate the contributions made by dermatology and dermatologists to the problem of military dermatology and the contributions made by the Armed Forces to dermatology):

1. The Military Affairs Committee of the American Academy of Dermatology and Syphilology under the chairmanship of Arthur Curtis, together with similar committees of other societies.

2. The Armed Forces Institute of Pathology, which has done much toward the elevation of histopathology as a science. Mention should be made of the civilian consultants to this body, such as Dr. Montgomery and Dr. Weidman.

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1. Manual of Dermatology: National Research Council, Division of Medical Sciences, by D. M. Pillsbury, M. B. Sulzberger, and C. S. Livingood, Philadelphia, W. B. Saunders Company, 1942, p. 421.

2. Pillsbury, D. M., and Livingood, C. S.: Experiences in Military Dermatology: Their Interpretation in Plans for Improved General Medical Care, Arch. Dermat. & Syph. **55**:441-458 (April) 1947.

3. The sponsorship of the Earl Osborne Fellowship to the Armed Forces Institute of Pathology under the auspices of this Academy.

4. Discussions and symposia of the type carried out at the annual meeting of the American Academy of Dermatology and Syphilology. It may be suggested that retirement points be given to those reserve officers attending such symposia.

5. The new section of Military Medicine of the American Medical Association. While not dermatologic, this is important, as is also the inclusion of representatives of the Armed Forces, Veterans Administration, and United States Public Health Service to the House of Delegates of the American Medical Association.

6. The facilities offered by the Armed Forces for postgraduate training in dermatology leading to board qualification. At the present time the Armed Forces offer training in dermatology as indicated in Table 1.

All but two of the residencies indicated in this Table are now filled, but there is increasing difficulty in filling these appointments. There is a total of 37 certified dermatologists now on duty in the Armed Forces. In addition, there is a total of

TABLE 1.—*Residencies in Dermatology Provided by the Armed Forces*

Service	Hospital	Training Given, Yr.	Residencies
Army	Brooke	3	3
	Walter Reed	3	6
	Letterman	3	3
Navy	U. S. Naval, San Diego	2	2
	U. S. Naval, Philadelphia	2	3
	U. S. Naval, St. Albans, N. Y.	2	2
Air Force *	Civilian hospitals chosen at discretion of Surgeon General	3	2

* Air Force is also allotted two of the Army residencies.

88 physicians in the Armed Forces who have had varying degrees of dermatologic training, and who, for the most part, are engaged in the practice of dermatology. Inasmuch as these figures are recent but not current, it may be that some of these 88 physicians reported to have less than board training in dermatology may have since become certified dermatologists.

7. The 15 full-time physicians within the Veterans Administration who are certified by the American Board of Dermatology and Syphilology. In addition, many Veterans Administration stations have part-time attending and consultant dermatologists, almost all of whom are certified. Then, too, in each region of the Veterans Administration are found one or more civilian certified dermatologists who act in a consultant and advisory capacity. The importance of dermatology and syphilology within the Veterans Administration is realized readily when it is known that as of Sept. 30, 1951, the monthly value of awards to 52,632 veterans of World War II whose major compensable disability was a dermatologic condition (exclusive of scars caused by injury) was $1,369,246. A slight increase in payments has occurred since July 1, 1952, as a result of Public Law 356. During the calendar year 1951, a total case load (primarily dermatologic or syphilologic) of 18,112 patients existed; the average duration of hospitalization was 67 days. An additional 17,608 patients had associated dermatologic diseases. The Veterans Administration

also provides postgraduate training in dermatology leading to board qualification through the various Deans Committees.

8. The awareness of the United States Public Health Service of its problems. At present (Oct. 9, 1952) 12 dermatologists in the United States Public Health Service are certified. Two dermatologists in the Division of Occupational Health spend 60% of their time in research. Five work in clinical dermatology and venereology in Public Health Service hospitals. One teaches in the School of Medicine in Rangoon, Burma, as part of the department of dermatology. Four are on active duty in the Venereal Disease Division; two of these are assigned to the Venereal Disease Research Laboratory and spend most of their time in research, one is assigned to the medical center at Hot Springs, Arkansas, where he spends most of his time teaching and doing research and clinical work, and one is assigned as Venereal Disease Control Officer to a large metropolitan region.

9. Representation of dermatologists on various subcommittees of the National Research Council.

TABLE 2.—*Morbidity Rate for Dermatologic Conditions: June, 1951, to July, 1952 (Annual Rates per 1,000 Mean Strength)*

	Skin and Cellular Tissue		Dermatophytoses		Scabies	
Service	Korea	World	Korea	World	Korea	World
Army	51.15	38.19	4.72	3.41	1.11	1.07
Navy	35.0*	23.0	2.0*	2.0	0.3*	0.3
Air Force	37.4	27.0	4.2	3.0	1.4	0.56

* Approximate.

10. The more active participation of military dermatologists in such activities as meetings, lectures, and exhibits. However, in this connection still more should be done; at the annual medicomilitary symposium for the Armed Forces held Oct. 20 to 25, 1952, at the United States Naval Hospital, Philadelphia, I was able to find but one and a half hours assigned to dermatology, and this time was devoted to two minor subjects.

Numerous current problems exist that must be considered from both civilian and military standpoints. In the last war cutaneous disease was the cause of evacuation of 14 to 16% of all patients sent back to the United States; in many overseas dispensaries as many as 75% of those reporting to sick call suffered from disease of the skin. These facts make it obvious that much remains to be done, and that this can be done only by means of education and research.

Even now diseases of the skin are an important factor in disability. The morbidity rate of dermatologic conditions in the current Korean situation is given in Table 2, together with the current world-wide rate. Several points of interest are evident in this study, one being that the rate of diseases of the skin and cellular tissues in the Army in Korea at present is almost identical with that in 1944 and 1945. However, the rate of dermatophytosis and scabies is considerably less. Also of interest is the fact that the rate for all dermatologic conditions in the Army in Korea is greater than that in other services; this is undoubtedly because of the number of Army personnel in the front lines.

Table 3 indicates the per cent of examinees who are being rejected because of dermatologic conditions, either primary or associated with other disorders. The Army and Air Force are grouped together because the Army handles all inductions for the Air Force. The percentages given are of those who have cutaneous diseases at the time of rejection, although other physical and mental defects may also be present. A rough estimate of the per cent of rejectees for cutaneous diseases alone is approximately two thirds of these figures.

In my opinion, the number of examinees rejected is less than it should be; those of us in World War II remember that many men received certification of disability discharges shortly after induction because of dermatologic disease or defects not properly appraised or recognized at the time of induction.

Dermatologic education is not only for medical officers of company grade, but should be available for those of flag or general rank, although, to my mind, such education should differ. To those of company or field grade, education should be directed along lines of basic dermatologic diagnosis, care, treatment, and prognosis. That a certain amount of this is being done is apparent from previous remarks regarding postgraduate training, yet the medical officer to whom this statement

TABLE 3.—*Per Cent of Examinees Rejected in Whom Cutaneous Disease Is a Principal Defect*

Service	Per Cent Rejected: Cutaneous Disease and Other Defects	Per Cent Rejected: Cutaneous Disease the Sole Defect
Army and Air Force	0.53	0.34 *
Navy	0.43	0.28 †

* Includes rejection for disfiguring scars. Rejections for cutaneous diseases excluding scars 0.24 per cent.
† Approximate.

now applies is usually not, and should not be, a dermatologist. He is the general medical officer in small station hospitals, dispensaries, divisional medical staffs, and the like.

How is he to receive this basic knowledge? First, fundamental education in the medical schools throughout the United States should provide more time for teaching in dermatology. It is a sad commentary on this specialty that many excellent schools of medicine devote but few hours to dermatology. This lack has been mentioned and stressed by leaders in dermatology time and time again, but little has been done. This should be a challenge to us as civilian dermatologists. It may be easy to criticize the military for things done and not done, but let us recognize here and now that much of the lack of undergraduate dermatologic education is our own fault and ours alone.

What can the Armed Forces do to stimulate dermatologic education? First, the previously mentioned facilities for postgraduate training in dermatology must be continued, but in addition provision must be made for the dermatologic training of general medical officers. This may be done through basic, so-called refresher courses in dermatology, not unlike those given in previous years by the University of Minnesota at its Center for Continuation Study. The American Academy of Dermatology and Syphilology might also consider this within its realm and provide such a course during the annual session. Such courses also could be given at the larger permanent hospitals of the Armed Forces.

Second, medical officers of higher rank should be made more aware of present dermatologic problems. Pillsbury and Livingood discussed this aspect at length, but yet little appears to have been done. I quote from Casberg [3]:

> In regard to high-level planning, the three Surgeons General have professional divisions in their office with representatives devoted to evolving policies for the intelligent utilization of the specialties concerned. In all three services it has been found uneconomical to have a dermatologist assigned full time to the administrative staff, and therefore, provisions are made whereby dermatologists assigned to Walter Reed Army Medical Center, U. S. Naval Medical Center, Bethesda, Maryland, or, if necessary, civilian consultants may be called to give advice whenever a question concerning this specialty arises.

I cannot agree completely with this. If the figures for disability and morbidity cited previously are true, and from my own experience I consider them to be conservative, it appears that a dermatologist of proved ability should be in a position of greater authority as far as high-level planning is concerned.

The Armed Forces, together with the Veterans Administration and United States Public Health Service are in a splendid position to conduct research by themselves or in cooperation with civilian institutions. Pillsbury and Livingood stated that a disproportionate amount of time is spent in investigation of diseases that are responsible for an infinitesimal proportion of the total disability from dermatologic disease and indicated further the unsolved problems of dermatologic therapy that were most obvious. These are in brief: (1) chronic pyogenic and fungous infections, (2) inadequate methods for control of pruritus, (3) lack of knowledge concerning eczematous eruptions of hands and feet, (4) inadequate methods for prevention of harmful effects of tropical exposure, (5) lack of methods for protection from contact dermatitis, (6) lack of methods for treatment of warts, especially plantar warts, (7) lack of satisfactory methods for treatment of chronic allergic states, severe acne, psoriasis, and seborrheic dermatitis, and (8) relative lack of scientific approaches to the study and management of psychosomatic states in chronic dermatoses.

Now, more than six years later, no material advance has been made in knowledge in most of these categories. This list is quite similar to that presented by Olansky [4] when he considered dermatologic conditions that lend themselves to public-health methods; he included tinea capitis, pyoderma, creeping eruption, moniliasis, psoriasis, acne, and atopic dermatitis. The similarity of the two lists is apparent. In this "atomic age" ionization damage and effects should also be considered proper fields for research.

Here, then, are obvious opportunities for research of paramount value to all, whether in civilian or in military life. The solution of such problems in research, however, is not so obvious and relates to the basic physiology of the skin, of which little is understood. Funds are available for research and it is a sad reflection to note that less than 1% of all such funds is being used presently for research in dermatology.

While unification of the services exists to a great extent, nevertheless items of supply are still available to medical officers of the Navy and the Air Force that are not available to Army officers. It is inconceivable that the type of work in the

3. Casberg, M. A.: Personal communication to the author.
4. Olansky, S.: Personal communication to the author.

three services varies to such an extent that this is necessary. It should also be noted that standard equipment for dermatologic care and diagnosis is not available in the Medical Supply Catalogue; I refer to such items as the Keyes punch for biopsy, skin curets, and Wood's light. Such lack should be corrected. Of course, funds are available in all hospitals for the purchase of nonstandard items, yet it might be more economical to have these items available in the Medical Supply Catalogue.

In conclusion, it is apparent that much has been done in the past 10 years to solve the problems of military dermatology. Problems still remain and always will, but with greater education and research by civilian dermatologists and those in the Armed Forces, Veterans Administration, and United States Public Health Service working together, much may be done to alleviate the condition of those afflicted with dermatologic disease and to reduce disability and morbidity rates of diseases of the skin. These are our common goals.

PHYSICAL ALLERGIES

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GENERALLY speaking, the physical allergies deal with those reactions of hypersensitiveness due to cold, heat, radiant energy, pressure, and mechanical stimuli. I am particularly concerned in this study with those reactions due to heat and cold. However, before going on to my subject I should like to mention that reactions of hypersensitiveness occur occasionally with roentgen, grenz, and radium irradiation, in addition to the rays of the visible spectrum, and it is important to note that certain instances of so-called photosensitivity really are due to the heat of such energy rather than the light per se.

If we are to accept the reactions of hypersensitiveness to heat and cold as truly allergic we must use the term broadly and in the sense originally defined by von Pirquet, that is, as an "altered capacity to react." Almost no one, however, agrees with this broad concept, but the feeling persists that the allergic state requires an antigen-antibody reaction and that it should be possible to demonstrate the existence of these antibodies by passive transfer or by other techniques.

Proof of an antibody-antigen mechanism is not possible in many reactions of hypersensitiveness, including reactions to heat and cold. Rajka and Asboth[1] demonstrated, by means of a so-called reagin-increasing method, positive Prausnitz-Küstner reactions in all four of their patients who were hypersensitive to cold. In this method, blood is taken after the patient's exposure to cold, when the serum contains more reagin, and by a reagin-fixation method the serum is injected into an area previously cooled with ice; the reaction gives positive results in instances in which the usual Prausnitz-Küstner test has failed.

Because of this controversy and because of doubt in the minds of many authorities regarding instances of hypersensitivity to cold and heat in which passive transfer of antibodies supposedly has been demonstrated,[2] the evidence has not impressed

From the Section of Dermatology and Syphilology, Mayo Clinic.

Read at the meeting of the American Academy of Dermatology and Syphilology, Chicago, Dec. 10, 1952.

1. Rajka, E., and Asboth, A.: Cold Urticaria: Investigations Concerning Its Pathogenesis, Ann. Allergy **9**:642-652 (Sept.-Oct.) 1951.

2. (*a*) Rajka and Asboth.[1] (*b*) Rothman, S., in discussion on Rodin, H. H.: Sensitivity to Cold, A. M. A. Arch. Dermat. & Syph. **63**:155 (Jan.) 1951. (*c*) Urbach, E.; Herrman, M. F., and Gottlieb, P. M.: Cold Allergy and Cold Pathergy, ibid. **43**:366-374 (Feb.) 1941. (*d*) Urbach, E., and Gottlieb, P. M.: Allergy, Ed. 2, New York, Grune & Stratton, Inc., 1946, Chap. 17, pp. 409-434. (*e*) Melczer, N., and Wlassics, T.: Über die Wärmeüberempfindlichkeit, Arch. Dermat. u. Syph. **176**:157-166 (Oct.) 1937.

many authorities, among them Rostenberg,[3] Sulzberger and Baer,[4] and Urbach and co-workers.[2c,d] Perhaps it is best to speak of such reactions as heat or cold hypersensitiveness rather than heat or cold allergy, at least until the day comes when these reactions are proved beyond doubt to fulfill the requirements of the allergic state. Duke,[5] in his original article on the subject, questions whether or not his cases are actually cases of allergy.

It might be of interest to review Duke's [5] original article wherein he stated that there are two distinct types of reaction: (1) a local contact type of reaction in which the area of exposure is delineated sharply, and (2) a diffuse reflex type of reaction.

The contact reactions produced by cold, freezing, burns, and mechanical irritation represented a distinct type of reaction characterized by the following phenomenon: 1. The patient gave a familial history of hay fever and asthma or hives or both. 2. A local reaction characterized by erythema, itching and edema was brought out specifically by the use of one or two agents but could not be produced by other agents. 3. The reaction failed to spread with pseudopod formation beyond the area directly exposed. 4. The skin was exhausted locally by reaction. 5. Local tolerance followed frequent exposures. 6. Symptoms of constitutional reaction, such as collapse, abdominal cramping, and eosinophilia, occurred after local reactions extending over large parts of the body. 7. Reactions, although stopped locally by an injection of epinephrine, were not affected by the subcutaneous injection of ordinary amounts of epinephrine at distant points.

The diffuse type of reaction caused by exposure to heat stands in striking contrast to the contact type of reaction in the following respects: 1. The redness, itching, and urticaria produced by heat spread very rapidly, involving almost the entire body within a few seconds. The local reaction at the site of application of heat was not much greater than the reaction that occurred generally. 2. The reaction was followed by temporary exhaustion of the skin, lasting up to several hours (five hours in the case of Peters and Silverman [6]). 3. The reaction could be stopped or prevented by the application of cold to the skin or by the subcutaneous injection of epinephrine. 4. The reaction could be produced by either mental or physical effort when the patient was warm. 5. The reaction was elicited even when tourniquets were tightly applied above the area exposed to heat.

It is surprising that our knowledge concerning these physical phenomena has advanced but little since Duke's [5] original paper.

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3. Rostenberg, A., Jr., in discussion on Rodin, H. H.: Sensitivity to Cold, A. M. A. Arch. Dermat. & Syph. **63**:154 (Jan.) 1951.

4. The 1951 Year Book of Dermatology and Syphilology, edited by M. B. Sulzberger, and R. L. Baer, Chicago, The Year Book Publishers, Inc., 1951, pp. 182-186.

5. Duke, W. W.: Urticaria Caused Specifically by the Action of Physical Agents (Light, Cold, Heat, Freezing, Burns, Mechanical Irritation, and Physical and Mental Exertion), J. A. M. A. **83**:3-8 (July 5) 1924.

6. Peters, G. A., and Silverman, J. J.: Role of Histamine and Acetylcholine in the Mechanism of Heat Allergy: Report of Studies on a Soldier, Arch. Int. Med. **77**:526-543 (May) 1946.

HYPERSENSITIVITY TO HEAT

Certain excellent articles[7] have reviewed and extended our knowledge of reactions by hypersensitivity due to heat. Identical reactions are due likewise to exertion and psychogenic factors. It is Duke's diffuse reaction to heat, exertion, and psychic stress that is now spoken of as "cholinogenic urticaria." "Cholinogenic urticaria"[7d,e] and "cholinogenic itching"[7c] are perhaps preferable terms in that the attacks may be produced at will by the administration of acetylcholine derivatives. Hopkins and associates[7d] first designated the term "cholinogenic urticaria," while Nomland[7c] added "cholinogenic itching" to designate the intense pruritus without urticaria which developed when the patients were exposed to heat, exertion, or emotional stress. Grant and co-workers[7e] postulated that acetylcholine and pilocarpine act through the parasympathetic nervous system—that is, the cholinergic nerves—to release H substance, which produces the urticaria. This theory, according to Nomland, is tenable concerning cholinogenic urticaria, but it does not explain cholinogenic itching, which also is produced by similar drugs and which he feels results from direct action on the cholinergic nerves of the skin.

According to Hopkins, the lesions of cholinogenic urticaria are characteristic. A bright red pruritic flare appears first and measures 2 to 5 cm. in diameter, and then in the center of the flare a small round wheal, 2 to 4 mm. in diameter, appears. Confluence of flare may be seen, but only rarely do wheals fuse; pseudopods are inconspicuous. Angioneurotic edema may be present. Sigel's[8] patients did not always have erythema.

Systemic manifestations, such as abdominal cramping, diarrhea, faintness and weakness, sweating, flushing, and salivation, are encountered frequently. These manifestations vary in the degree of severity, and at times collapse occurs. All are similar to the physiologic effects of pilocarpine.

In the series of cases reported by Hopkins[7d] the most frequently cited causes of reactions were taking hot baths, remaining in warm rooms, exposure to summer sun, standing in front of a fire or over a cookstove, or eating hot foods. Twelve patients felt that attacks were brought about by physical exertion, and 12 recognized that psychic stimuli caused reactions. Three patients stated that their attacks were worse in the summer, three stated that they were worse in the winter, and two stated that a sudden change from cold to hot weather produced especially severe attacks. There was often evidence that cold was an additional cause of outbreaks.

Hopkins also differentiated clearly the local contact type of urticaria from the generalized cholinogenic type. Immersion of one hand and forearm of a patient with the contact type in water at 100 F. (about 38 C.) for five minutes produced

7. (*a*) Melczer and Wlassics,[2e] (*b*) Peters and Silverman,[6] (*c*) Nomland, R.: Cholinogenic Urticaria and Cholinogenic Itching, Arch. Dermat. & Syph. **50**:247-249 (Oct.) 1944. (*d*) Hopkins, J. G.; Kesten, B. M., and Hazel, O. G.: Urticaria Provoked by Heat or by Psychic Stimuli, ibid. **38**:679-691 (Nov.) 1938. (*e*) Grant, R. T.; Pearson, R. S. B., and Comeau, W. J.: Observations on Urticaria Provoked by Emotion, by Exercise and by Warming the Body, Clin. Sc. **2**:253-272 (July) 1936.

8. Sigel, H.: Urticaria Caused by Heat, Exertion and Excitement: Report on 22 Cases Among American Soldiers in Japan, Arch. Dermat. & Syph. **57**:204-209 (Feb.) 1948.

flushing of the exposed area at withdrawal, followed in five minutes by a uniform tense wheal. There were no wheals or flares elsewhere. In the contact variety urticarial lesions developed only on the area of the skin which was exposed.

Under controlled conditions, a patient studied by Peters and Silverman[6] exhibited definitely delayed sweating responses over the entire surface of his body, although palmar sweating was normal at all times.

The diagnosis of cholinogenic urticaria may be made in most instances by a thorough evaluation of the history, not only with respect to heat but also with respect to exertion and psychic stimuli, together with inspection of the lesions during an attack. If the diagnosis is doubted, it may be confirmed by the administration of acetylcholine derivatives, such as methacholine (Mecholyl) (administered subcutaneously, intradermally, or by iontophoresis), or of pilocarpine, or even by the actual application of heat.

Treatment is disappointing frequently. The physiologic antagonists of acetylcholine and pilocarpine, such as atropine, produce little benefit. Nomland stated that atropine in sufficient dosage to produce its own physiologic effects gave little if any benefit or protection to such patients, although in one case theophylline brought about a less severe attack after an attack produced by methacholine. Attempts to desensitize patients by gradual increments of methacholine have failed. Peters and Silverman reported a case in which epinephrine, atropine, and histamine inhibited the development of exertional and heat urticaria, while ephedrine administered in the usual doses did not. In the same patient, pilocarpine alone or furtrethonium (Furmethide) iodide (furfuryltrimethylammonium iodide, related chemically to acetylcholine) alone did not provoke urticaria, but the two given 25 minutes apart did produce urticaria, as did the combination of histamine and furtrethonium (Furmethide) iodide.

My colleagues and I have found that treatment with the so-called antihistaminic preparations occasionally has alleviated an acute episode, but it has not prevented the development of future attacks. Other preparations, such as ephedrine and epinephrine, may produce some amelioration, but the effects cannot be anticipated for any particular patient. Attempts at desensitization by means of immersion of one part of the body, such as a hand or forearm, in water of gradually increasing temperature occasionally may produce satisfactory results. First the temperature of the water is below the threshold at which symptoms are produced, usually at body temperature, and then the temperature of the water is increased gradually up to that which produces symptoms. The temperature is then decreased and very gradually increased again, in the hope that the threshold level can be passed and that the patient ultimately will be desensitized to the effects of heat. The same type of treatment is applicable to those who have the local contact type of hypersensitivity to heat. Oftener than not, however, patients with this disorder have learned from experience how to abort an attack by means of rest and the application of cold water or ice. They also have learned from experience what their own threshold is for various forms of heat, exertion, or physic stimuli, and beyond which they cannot go. This aspect is emphasized further when conferring with the patient, and if he is cooperative much benefit may be obtained.

HYPERSENSITIVITY TO COLD

The reactions to cold were generally described by Duke [7] when he defined the contact type of reaction. The clinical appearance is that of a sharply delineated flare associated with formation of a wheal but again with few pseudopods. The whealing, however, is much greater than that seen in the diffuse reaction to heat.

Ever since Horton [9] originally, in 1927, and later in greater detail, in 1936, described the syncopal episodes and constitutional collapse in such patients while swimming (which may cause drowning), there has been an increased awareness of this manifestation of hypersensitivity to cold. According to Horton, these local and systemic reactions are similar to those produced by the injection of histamine or of histamine-like substances, and consist for the most part of urticarial lesions over the exposed areas of the body. A number of patients have dysphagia, swelling of the mucous membranes, and abdominal cramping after the ingestion of cold liquids. The majority of Horton's patients had severer systemic reactions consisting of syncope, and some remained unconscious for more than two hours. Syncope developed in 15 of 18 patients after swimming, and 4 of them had had to be rescued.

Local and systemic reactions were produced in certain of these patients by immersion of the hand in water at 8 C. for periods of six minutes. The local effects consisted of pallor during the period of immersion followed by redness, swelling, and increased local temperature on removal of the exposed part from the cold water. After a latent period of from three to six minutes the characteristic systemic reactions developed, consisting of a sharp fall in blood pressure, a rise of the pulse rate, flushing of the face, a tendency toward, or the actual development of, syncope, and recovery from the reaction after 10 to 15 minutes. The systemic reaction did not develop if a tourniquet was applied so as to exclude the return of venous blood from the immersed part or lessen the supply of arterial blood to the hand before it was immersed in cold water, or if the tourniquet was applied and kept on after removal of the hand from the cold environment. However, when the tourniquet was finally removed the systemic reactions were severer, frequently lasting three times as long as when the tourniquet was not used. Horton felt that this observation was an important one, and it seemed to eliminate the possibility of a reflex basis to the systemic response. Other systemic manifestations have been ascribed to cold, including edema of the glottis, diarrhea, visual disturbances, purpura, and non-infectious diseases of the perinasal sinuses, which may be attributed to a localized urticarial reaction in the nasal tissues. Williams [10] suggested that myalgia involving the muscles of the head is on a similar basis. Other disorders, including nausea, vomiting, irritable bladder, arthralgia, and vertigo, are thought to be due basically to reactions of hypersensitivity to cold. Hemoglobinuria may be present.

Apropos of certain atopic features first mentioned by Duke,[7] although not by this term, it might be stated that many patients have a definite genetic background

9. (*a*) Horton, B. T.: Cold Allergy: Report of 2 Cases, Proc. Staff Meet., Mayo Clin. **2**:276-278 (Nov. 23) 1927. (*b*) Horton, B. T.; Brown, G. E., and Roth, G. M.: Hypersensitiveness to Cold, with Local and Systemic Manifestations of a Histamine-Like Character: Its Amenability to Treatment, J. A. M. A. **107**:1263-1269 (Oct. 17) 1936.

10. Williams, H. L.: The Syndrome of Physical or Intrinsic Allergy of the Head: Myalgia of the Head (Sinus Headache), Proc. Staff Meet., Mayo Clin. **20**:177-183 (June 13) 1945.

of familial hypersensitivity to cold,[11] and in such cases this hypersensitiveness to cold is present as a dominant non-sex-linked Mendelian trait. These reports demonstrate that approximately 50% of the members of such families have similar signs and symptoms.

It has been shown [9a] that previous mechanical stimulation or trauma renders the skin more reactive than it otherwise would be.

Rostenberg,[3] as well as others, has shown that the critical temperature at which symptoms develop varies considerably. It appears that there must also be a temperature gradient; in other words, a sudden drop of temperature to a certain level in the summertime will produce symptoms, yet the same temperature level will not produce a reaction in the winter months. The same temperature gradient seems to apply also to instances of hypersensitiveness to heat.

The diagnosis of hypersensitivity to cold is usually simple in the presence of a well-established and correlated history. However, confirmatory tests may easily be made by the application of cold water contained in a test tube to a part of the body, or the immersion of a hand or forearm in cold water at 6 to 10 C. for 6 to 10 minutes.

Treatment involves primarily the avoidance of such exposures, although attempts at desensitization may be made in a manner similar to that suggested for desensitization to heat, in that a part of the body may be immersed in water, the temperature of which is above the reactive level. The temperature is gradually reduced, and it is hoped that in this manner the body will become desensitized. Such "autodesensitization" may be attempted by immersing the patient's foot or hand in water at 17 C. (about 63 F.) for two to five minutes one or more times daily and gradually reducing the temperature of the water to a minimum of 7 C. (about 45 F.) over a period of three to four weeks. If reactions occur during treatment heat may be applied.

Nicotinic acid (niacin) has been found effective by Williams [10] in his group of patients, 200 mg. daily generally being an adequate dose.

It also has been shown that the antihistaminic group of preparations may be effective. Horton and his associates [9b] have recommended injections of histamine in dosages of 0.1 mg. or less twice daily for two or three weeks.

DERMOGRAPHISM AND PRESSURE URTICARIA

Urbach and Gottlieb [2d] do not feel that dermatographism or factitial urticaria is to be regarded as a physical allergy, but rather as vasomotor neuropathologic conditions which may be due to traumatic release of H substances. Rasmussen,[12] investigating the action of antihistaminics on histamine whealing and dermographism concluded that the similarity of results obtained supported the theory that dermographism is produced by liberation from injured cells of a histamine-like

11. (*a*) Urbach and co-workers.[2c, d] (*b*) Rodin, H. H.: Sensitivity to Cold, A. M. A. Arch. Dermat. & Syph. **63**:152-154 (Jan.) 1951. (*c*) Witherspoon, F. G.; White, C. B.; Bazemore, J. M., and Hailey, H.: Familial Urticaria Due to Cold, ibid. **58**:52-55 (July) 1948. (*d*) Kile, R. L., and Rusk, H. A.: A Case of Cold Urticaria with an Unusual Family History, J. A. M. A. **114**:1067-1068 (March 23) 1940.

12. Rasmussen, K. A.: The Effect of Antihistaminics on Histamine Whealing and on Dermographism: Elucidated by Comparative Electrophoretical Experiments, Acta dermat.-venereol. **29**:564-571, 1949.

substance; in other words, his findings are similar to those of Urbach. Patients afflicted with dermographism usually do not have other types of urticaria, that is, those due to food or cold or the cholinogenic type. Some persons have intense pruritus in the traumatized areas, while others do not have any subjective symptoms whatsoever. To those patients with symptoms the antihistaminic group of drugs frequently give relief, as well as preventing or inhibiting the wheal and flare response.

The same controversial problems concerning pathogenesis face the investigators of dermographism, most of whom feel that the condition is due to liberation of a histamine-like substance from cells as a result of the mechanical injury; others have been able to demonstrate passive transfer antibodies.

Dermographism must be differentiated from pressure urticaria. The former appears abruptly or within comparatively few minutes after relatively insignificant trauma and subsides within an hour—although persistent and delayed reactions have been reported.[13] Pressure urticaria is a delayed reaction appearing only after latent periods of several hours, persisting and appearing only at the site of relatively great pressure. In the case of persistent and delayed dermographism referred to, pressure urticaria also was demonstrated and was present, with vesiculation in the area to which the strap and weight of a golf bag had been applied for several hours.

Urbach and his associates mentioned instances of pressure urticaria exhibiting its symptoms only when the patient was suffering from acute or chronic gastrointestinal disease.

COMMENT

There are factors present within all of us which may make us either more sensitive to the effects of certain physical agents or more resistant. Duke and many others have shown that many patients become sensitive or more sensitive to the physical agents while they are suffering from hay fever due to pollen. It has been shown likewise that a febrile illness may "exhaust" the skin so that it is more resistant to the effects of physical agents.

Urbach, in attempting to explain the various phenomena of physical hypersensitiveness, mentioned five possible mechanisms of action. The first is that of a primary physical allergy operative on the basis of specific antigen-antibody reactions, which he feels is an infrequent circumstance. The second explanation also is basically that of allergy, in which the antigen is autogenous and perhaps is some chemical or physicochemical alteration of the protein in the tissues. In this connection Sherman and Seebohm[14] were able to fractionate the serum proteins of a patient with cold hypersensitiveness. The individual fractions were not antigenic by the passive transfer technique, but certain mixtures of the fractions were.

The third mechanism is that of histamine effect due to the liberation of histamine-like substance from the injured tissues. This theory has received support from many investigators.

The fourth possible mechanism of action is that which Urbach designated "cold-specific vasomotor neuropathy" or, more simply, as "cold pathergy," in which it is assumed that instability of the central or peripheral vasomotor mechanism may be responsible for the abnormal neurovascular response to local physical agents.

13. Kalz, F.; Bower, C. M., and Prichard, H.: Delayed and Persistent Dermographia, Arch. Dermat. & Syph. **61**:772-780 (May) 1950.

14. Sherman, W. B., and Seebohm, P. M.: Passive Transfer of Cold Urticaria, J. Allergy **21**:414-424 (Sept.) 1950.

Williams,[15] in attempting to explain the various manifestations of the allergic response and of hypersensitiveness, has implicated the autonomic nervous system as being the pathway or mediator by which the target organ or organs are reached.

Finally, there may be central disturbances of the temperature-regulating mechanism producing pathologic reactions in the blood vessels of the skin. Duke favored this concept in explaining his "reflex-like" reaction.

While all these possible mechanisms have their supporters, nevertheless, it still is not known with certainty which of them actually plays the greatest role in the production of hypersensitiveness to physical agents.

15. Williams, H. L.: A Concept of Allergy as Autonomic Dysfunction Suggested as an Improved Working Hypothesis, Tr. Am. Acad. Ophth. **55**:123-146 (Nov.-Dec.) 1951.

ETIOLOGY OF NUMMULAR ECZEMA

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NEARLY 100 years have elapsed since Devergie [1] described nummular eczema. Since then, nummular eczema has been confused with other disease entities and has been described under such names as orbicular eczema, parasitic eczema, and herpetoid eczema. Devergie was not the first to compare plaques of dermatitis to coins. Rayer,[2] in referring to what must have been nummular eczema, stated: "This variety is distinguished by clustered patches of vesicles, the dimensions of which vary from those of a sovereign to those of a two sovereign piece." In Rayer's book there was an illustration showing the radial side of a hand with typical coin-sized plaques of dermatitis.

Characteristically, nummular eczema occurs in sharply defined coin-sized vesicular plaques favoring the extensor surfaces of the extremities below the knees and the elbows. The best descriptions of nummular eczema which we have found to date are those by Sulzberger and Wolf [3] and by Gross.[4]

Our preliminary work for this study was based on studies of 600 patients with an eruption of the hands, in which 178 patients with nummular eczema were compared statistically with those having other types of dermatitis. As a result of this study we came to the conclusion that the causes of nummular eczema are multiple, and that the clinical picture is dependent upon the interaction of three etiological components, which we conceive to be (1) nutritional, (2) allergic, and (3) infective.

In our series of patients with nummular eczema the female patients slightly outnumbered the male patients. Although the greatest number of patients were in the third decade of life, all ages were represented. In many patients the eczema was initiated by a frank dermatitis venenata, or allergic contact type of dermatitis. In a few patients nummular eczema began in the lesions of scabies.

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From the Health Service and Department of Bacteriology, Bucknell University.

1. Devergie, M. G. A.: Traité pratique des maladies de la peau, Ed. 2, Paris, V. Masson, 1857, p. 233.

2. Rayer, P.: A Theoretical and Practical Treatise on Diseases of the Skin, Philadelphia, Carey & Hart, 1845, p. 114.

3. Sulzberger, M. B., and Wolf, J.: Dermatologic Therapy in General Practice, Ed. 3, Chicago, Year Book Publishers, Inc., 1948.

4. Gross, P.: Nummular Eczema as a Clinical Entity, New York J. Med. **51**:2025 (Sept. 1) 1951.

NUTRITIONAL COMPONENT

Analysis of our records indicated that as a group the patients with nummular eczema tended to eat small quantities of meat and vegetables and large quantities of concentrated carbohydrates and fat. The nummular eczema group stood apart from other diagnostic groups by the high incidence of patients who did not eat meat daily or who actually disliked meat. Of those patients with nummular eczema who ate adequate amounts of meat and vegetables the majority also consumed excessive amounts (daily) of ice cream, candy, soft drinks, and other forms of concentrated carbohydrates and fat.

The tongue signs of vitamin B deficiency, such as marginal fluting, color changes, hypertrophied fungiform papillae, and angular stomatitis, were no commoner in the patients with nummular eczema than in patients suffering from chronic eczematoid dermatitis or atopic dermatitis. The incidence of tongue signs of vitamin B complex deficiency was, however, significantly higher in the nummular eczema group than in groups with eczematous eruptions classified as dermatitis venenata, or contact dermatitis.

We have occasionally seen an angry extensive eruption of nummular eczema develop suddenly in an older patient within a few weeks after all his teeth had been extracted. At first we thought that the outbreak was related to the absorption of bacterial products from the injured gingival areas, but the outbreak of eczema did not appear until healing was complete. It finally became evident that the sudden appearance of the eczematous eruption was precipitated by the enforced change in eating habits incident to the edentulous condition, in which less protein and more carbohydrate were eaten.

It has been known for years that patients who eat an excess of concentrated carbohydrates are often subject to furunculosis and pyodermas, and that their resistance to bacterial infection is low. Pillsbury and Sternberg [5] found that the course of an experimental infection in dogs was severer in those on a high-carbohydrate diet than in those on a low-carbohydrate or high-fat diet.

When it became apparent that the majority of our patients were poorly nourished, and that many had had inadequate diets with excessive amounts of carbohydrates for prolonged periods of time, we began to wonder if they might, as a group, have anemia. We postulated that if they had not eaten dark green vegetables and meat, which are good sources of folic acid, macrocytic anemia might have developed. Accordingly, we took blood cell counts of 35 consecutive patients with nummular eczema. Of this number in 25 (71%) the mean corpuscular volume was over 92 cubic micra, in 11 (31%) the hemoglobin content was below normal, and in 10 (28%) the red blood cell count gave below-normal results.

We classify the recurrent eczematoid affection of the hands described by Pollitzer [6] as nummular eczema with a strong nutritional component. All the patients

5. Pillsbury, D. M., and Sternberg, T. H.: Relation of Diet to Cutaneous Infection: Study of Influence of Varying Carbohydrate and Fat Intakes and of Fasting on Experimental Pyogenic Cutaneous Infections in Dogs, with Comparative Determinations of the Glycogen Content of the Skin and Liver, Arch. Dermat. & Syph. **35**:893 (May) 1937.

6. Pollitzer, S. A.: Recurrent Eczematoid Affection of the Hands, J. Cutan. Dis. **30**:716 (Dec.) 1912.

in our series with conditions which seemed to answer Pollitzer's description (3%) had marked anemia, mostly of the macrocytic type; all had eaten imbalanced diets, and one previously had had a gastrectomy. It is our impression that the incidence of alcoholism may be a little higher in this group of patients, but we do not feel that the histories in respect to alcohol were dependable.

ALLERGIC COMPONENT

Perhaps a better title for this section would have been "The Immunity Mechanism as a Component in the Etiology of Nummular Eczema," providing one is nimble-minded enough to accept allergy as a subdivision of immunity or to accept both immunologic and allergic processes as operating in the same plaque of nummular eczema.

We have used Staphylococcus vaccine-toxoid in the treatment of nummular eczema for many years. As a result of our experience with this treatment, we have come to appreciate the importance of allergy to the endotoxins of the Staphylococcus. In many patients with nummular eczema, Staphylococcus vaccine-toxoid can be administered in the same dose schedule as that used for the treatment of furunculosis. In those, however, who have become highly sensitized, the Staphylococcus vaccine-toxoid must be given in minute ascending doses with the same care and precautions used in administrating pollen extracts in the treatment of hay fever or asthma. A flare-up of the eczematous eruption appearing within 12 to 18 hours after an injection of Staphylococcus vaccine-toxoid indicates overdosing. Even though we have been cautious and have used small doses, we have produced these focal reactions with doses of Staphylococcus vaccine-toxoid of as little as 0.1 ml. of 1 : 10,000, 1 : 100,000, and even 1 : 1,000,000 dilutions.

The reaction that follows accidental injections of Staphylococcus vaccine-toxoid into the vein of a highly sensitized patient with nummular eczema is a generalized vesicular eruption without nummular configuration. We have seen this type of reaction appear spontaneously in patients with localized nummular eczema.

In our patients classified as having nummular eczema, the incidence of hay fever, asthma, migraine, urticaria, and infantile eczema appeared with slightly less frequency than in patients with dermatitis venenata, or contact dermatitis.

It is our belief that the plaques of nummular eczema represent islands of sensitized skin which are due most frequently to an allergy to the endotoxins of the Staphylococcus, sometimes to streptococci, and less frequently, to food proteins. The presence of annular lesions, the not uncommon occurrence of C-shaped lesions, and a distinct tendency for the nummular plaques to migrate slowly over the back of the hands are best explained by the development of local immunity. We have observed the C-shaped lesions most frequently in treated, partially healed processes. The tendency for the plaques to migrate may not be appreciated unless photographs or drawings are made periodically.

The incidence of tonsil infection was significantly high in patients with nummular eczema as compared with other groups. We relate the importance of foci of infections to the allergic component and believe that in nummular eczema the foci release allergens which activate the plaques of sensitized skin.

INFECTIVE COMPONENT

We found, in statistical studies (unpublished), that the incidence of Staphylococcus infections such as styes, furuncles, circinary impetigo, and osteomyelitis was significantly higher in nummular eczema than in other eczematous diseases. Many of our patients had active furuncles while under treatment for nummular eczema. Rayer [2] had observed the frequent association of impetigo and eczema. Around the turn of the century many investigators, notably Unna [7] and Engman,[8] regarded Staphylococci as the chief cause of eczema. The excellent work of Engman seems to have had more lasting influence than that of the earlier workers, because it was based on epidemiological considerations. After reading Engman's paper and thinking back over our earlier patients with nummular eczema, we recalled that many relatives and associates of these patients had consulted us for treatment of circinary impetigo, boils, nummular eczema, and chronic eczematoid dermatitis. Many of the patients with nummular eczema themselves had an associated impetigo of the ears, involving the helix and lobule. In recent years Lane and his co-workers [9] and Storck [10] have studied the bacterial flora of eczematous eruptions and have reaffirmed the etiological importance of bacteria in general and of staphylococci in particular.

In a series of 37 patients cultures were made from plaques of nummular eczema on blood agar (human) with a platinum loop. Of these, 27 grew Staphylococcus aureus, 8 showed nonhemolytic staphylococci, 4 showed nonhemolytic streptococci, and 6 showed β-hemolytic streptococci. These bacteriological findings were essentially the same as those reported in a series of 50 patients studied by Hopkins and Burky.[11]

We regarded the streptococci as secondary invaders, as did Hopkins and Burky.

The accumulation of evidence favoring the Staphylococcus as a cause of nummular eczema became so convincing that we decided to use a selective culture medium for the staphylococci and attempt to evaluate their role in a more positive manner.

MATERIALS AND METHOD

Small aluminum dishes 44 mm. in diameter and 6 mm. deep were used. These were autoclaved in 6-in. (15.2-cm.) Petri dishes. Mannitol salt agar (Difco) was used as a selective culture medium, and the dishes were poured brim-full. This required about 10 ml. of medium. A small amount of sodium chloride in the bottom of a small paper soufflé dish was placed in the center to attract water of condensation. In this way we usually had surfaces that were neither too wet nor too dry.

The medium is naturally red in color, and the organisms which ferment mannitol change the color to yellow. Phillips Thygeson,[12] in a study of conjunctival inflammation, found that this

7. Unna, P. G.: Parasitare Natur des Ekzems, Deutsche Med.-Ztg. **21**:809 (Aug.) 1900.

8. Engman, M. F.: An Infectious Form of an Eczematoid Dermatitis, Am. Med. **4**:769 (Nov. 15) 1902.

9. Lane, C. G.; Rockwood, E. M.; Sawyer, C. S., and Blank, I. H.: Dermatoses of the Hands, J. A. M. A. **128**:987 (Aug. 4) 1945.

10. Storck, H.: Experimentelle Untersuchungen zur Frage der Bedeutung von Mikroben in der Ekzemgenese, Dermatologica **96**:177, 1948.

11. Hopkins, H. H., and Burky, E. L.: Cutaneous Autosensitization: Role of Staphylococci in Chronic Eczema of the Hands, Arch. Dermat. & Syph. **49**:124 (Feb.) 1944.

12. Thygeson, P.: Mannitol Fermentation as an Indicator of Conjunctival Pathogenicity of Staphylococci, Arch. Ophth. **20**:274 (Aug.) 1938.

medium gave a reliable indication of probable pathogenicity of staphylococci when they were mannitol-fermentive. In the culturing process the plates were placed firmly against the skin for 10 seconds and then incubated for 48 hours at 32 C. The colonies which developed were then counted in respect to color, i. e., white or golden-yellow colonies, and in respect to mannitol fermentation. A Veeder counter was used to facilitate colony-counting. When the staphylococci were too numerous to count conveniently with a Veeder counter, a small measured area was counted and the total number for the whole plate was estimated.

CUTANEOUS FLORA OF A NORMAL SERIES

In order to establish norms we applied the mannitol salt agar plates to 100 persons who had no eruption of the skin. These were for the most part students

Fig. 1.—Aluminum spot plates and method of sterilization in large Petri dish.

attending Bucknell University. The plates were applied to three areas, namely, the cheek, the flexor surface of the forearm, and the dorsal surface of the hand. In this series of tests we rejected persons with acne and those who had recovered from acne.

As a result of this survey we found a wide variation in the number of colonies of so-called nonpathogenic staphylococci which did not ferment mannitol. The colony counts on contact cultures from the cheeks were usually higher than those in other areas. The yellow colonies, mostly pathogenic in type, were more constant than the white colonies, averaging four to six per plate. Mannitol-fermentive organisms were rarely found in this normal series as indicated by a change in color

of the medium from red to yellow. A statistical summary of this series is found in Table 1. The only significant differences between the means of this normal series

TABLE 1.—*Nonpigmented and Pigmented Staphylococci from 100 Normal Persons*

	White Colonies			Yellow Colonies		
Culture Site	Mean	Probable Error	Standard Deviation	Mean	Probable Error	Standard Deviation
Hands (dorsal surface)	21	± 1.4	30	4	± 1.2	16
Forearms (flexor surface)	29	± 5.3	77	5	± 1.5	22
Cheeks	55	± 5.0	75	6	± 1.6	23

Fig. 2.—Typical plaque of nummular eczema.

are between those of the white colonies, in the cultures taken from the hands, which had a mean of 21, and those from the cheeks, which had a mean of 53. Apparently, in many persons the greater number of sebaceous glands on the face provides more favorable growth conditions for the nonpigmented staphylococci (staphylococci epidermidis) than the skin on the dorsal surface of the hand.

NUMMULAR ECZEMA SERIES

This series included 81 patients with typical nummular eczema. Those with lesions involving chiefly the palmar or plantar surfaces were excluded. The cultures were taken by pressing the mannitol salt agar contact plate briefly against the

eczematous plaque and by applying another contact plate to an area symmetrical with the plaque if it was free of eczema and, if not, to an adjacent area of normal skin 7 cm. away from the lesion which had been cultured. Table 2 gives a statistical summary of these results, but it cannot convey the striking differences in color between the contact plates taken from the normal skin and those of the eczematous areas. The contrast is more striking when the cultured plaque is only a centimeter or so in diameter, in which case the size of the plaque shows on the plate as a mass of closely grouped yellow colonies on a yellow background surrounded by a red areola of the unaffected medium.

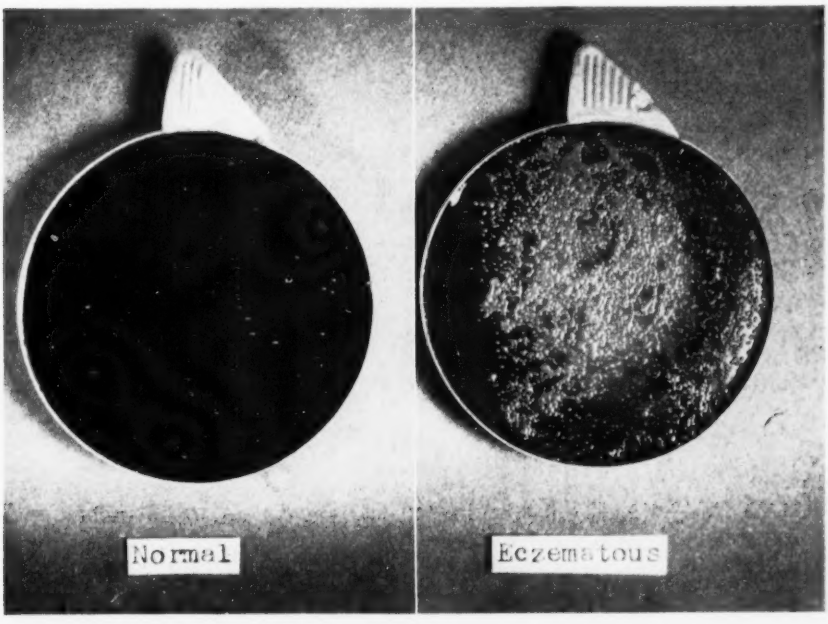

Fig. 3.—Mannitol plate exposed to normal and eczematous skin.

TABLE 2.—*Colonies of Mannitol-Fermentive Staphylococci from Patients with Nummular Eczema*

Source	Patients, No.	Mean Colonies, No.	Probable Error of the Mean	Standard Deviation
Normal	63	26.48	± 6.5	77.6
Eczematous	81	428.49	± 66.5	888.6

The difference between the means from the normal skin areas and those from the eczematous areas is highly significant, giving a value for "*t*" of 3.5, with a value of *P* at the 0.1% level ($P = 0.001$).

When our data were analyzed in respect to pigment formation in the Staphylococcus colonies, there was found to be no significant difference between the number of white colonies on the normal areas and those on the eczematous areas. The

relative number of pigment-producing colonies in the eczematous areas was extremely high. A statistical summary is found in Table 3.

The difference between the means of the yellow colonies from the normal and the means from eczematous areas give a "*t*" value of 3.9, with a value of *P* at the 0.1% level (*P* = 0.001).

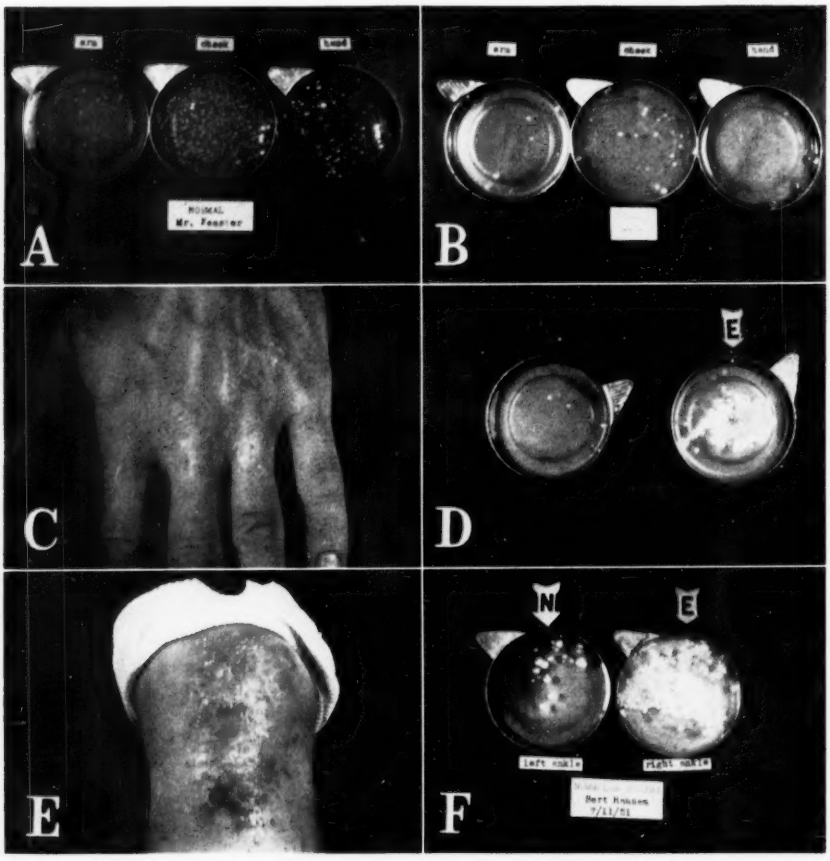

Fig. 4.—*A* and *B*, mannitol plates from normal patient; *C*, nummular eczema of the hands; *D*, mannitol plate from normal skin and eczematous plaques of above; *E*, nummular eczema of the lower tibial region; *F*, mannitol plates of normal and eczematous skin of above.

TABLE 3.—*Comparison of Nonpigmented and Pigmented Staphylococci from Patients with Nummular Eczema*

		White Colonies			Yellow Colonies		
Source	Patients, No.	Mean	Probable Error of Mean	Standard Deviation	Mean	Probable Error of Mean	Standard Deviation
Normal	63	33.6	± 4.65	55.4	22	± 4.4	61.8
Eczematous	81	41.9	± 17.6	235.6	463	± 31.8	424.8

RESULTS OF TEST IN ALLERGIC ECZEMATOUS CONTACT-TYPE DERMATITIS, AND DERMATITIS VENENATA

In order to show that all eczematous eruptions are not associated with an increased number of staphylococci on the skin, we tested all new patients with dermatitis venenata or allergic eczematous contact-type dematitis. The duration of the eruption in these patients was from one to five days. Patients who had dermatitis venenata for a week or more usually had a count above normal, but if a patient who had nummular eczema also acquired dermatitis venenata, the count usually increased rapidly.

COMMENT

Once it is granted that the pathogenic forms of staphylococci are significantly high in plaques of nummular eczema, it would seem that certain aspects of nummular eczema, which were formerly puzzling, can be readily explained. The peculiar response to therapy that has been noted by most authors can be, for the most part, explained on the basis of a staphylococcidal action. Iodochlorhydroxyquin (Vioform), which works well in nummular eczema, has a well-known staphylococcidal

TABLE 4.—*Nonpigmented and Pigmented Forms in 20 Patients with Dermatitis Venenata*

	White Colonies			Yellow Colonies		
	Mean	Probable Error of Mean	Standard Deviation	Mean	Probable Error of Mean	Standard Deviation
Normal	15.6	± 6.2	40.5	3.4	± 1.2	8.04
Eczematous	15.9	± 3.08	19.9	6.3	± 1.5	10.06

action. The use of the tars reduces the number of colonies of pathogenic staphylococci in the eczematous plaques. The antibiotics, providing the staphylococci are sensitive to them, when used locally are good remedies for the control of the infective component.

The eruption in many patients with nummular eczema clearly begins as dermatitis venenata or allergic eczematous contact-type dermatitis. These patients may say, "I acquired poison ivy last May and here it is November and I'm just the same." We have obtained this history so often that we now warn patients with nummular eczema to avoid risks of poison ivy, because it may require months to control the eruption. The invasion of the skin by staphylococci explains why nummular eczema begins at the sites of minor cuts, of burns, and the lesions of scabies.

Those patients whose nummular eczema develops in the wake of a compensable allergic eczematous contact-type dermatitis often cause embarrassment for the attending physician and the compensation adjustor. The course of the eczema may be prolonged beyond all reason when considered as an allergic eczematous contact-type dermatitis, and acute flare-ups may occur while the patient is at home, away from all industrial contactants.

We believe that there are types of nummular eczema representing the nutritional, infective, and allergic components. The Engman [5] type of chronic infectious eczematoid dermatitis is, so far as we can determine, identical with nummular eczema. We consider Engman's type as nummular eczema with an infective component greater than the nutritional or allergic components. We take the Pollitzer type [6] to

be nummular eczema with a predominating nutritional component. The generalized vesicular eruption, which occasionally occurs within a day after an injection of Staphylococcus vaccine-toxoid (accidental intravenous injections), represents an eruption with a predominating allergic component. More frequently, the type with a predominating allergic component may also have a focal flare-up with small doses of Staphylococcus vaccine-toxoid in 1 : 100,000 or 1 : 1,000,000 dilutions.

From the time of Unna [7] to that of the most recent workers, staphylococci have been thought by many to be the cause of eczema. Why then were staphylococci not accepted as playing a leading role in the etiology of nummular eczema? Was it because the same type of Staphylococcus was not always grown on culture or because streptococci and other micro-organisms were isolated at times from the nummular plaques? While the majority of staphylococci isolated from the nummular plaques do, as a matter of fact, satisfy the usual criteria of pathogenicity in that they hemolyze red blood cells, ferment mannitol, liquefy gelatin, and produce coagulase, we do not think that pathogenicity is essential. It is impossible to fulfill Koch's postulates in allergic disease. It is no more essential for staphylococci to be pathogenic in order to produce nummular eczema than it is for pollen grains to be pathogenic in order to produce hay fever. The cutaneous tests with Staphylococcus vaccine-toxoid did not show the high incidence of immediate reactions that one finds in testing patients with hay fever with pollen extracts, so perhaps this discrepancy has been one reason why the allergic component has not been accepted. We are not dealing, however, with atopy, but with a group of patients who have a low incidence of atopic diseases, so that the results of cutaneous testing of patients with nummular eczema and hay fever are not comparable. The delayed reactions to Staphylococcus vaccine-toxoid do not correlate in staphylococcic disease to the high degree that tuberculin tests do in tuberculous persons, but we do not believe that this rules out bacterial allergy as a factor in nummular eczema. We do, as Swineford and Holman [13] suggest, need better tests. The focal flare-up after an injection of Staphylococcus vaccine-toxoid is the only method we know that demonstrates the allergic component. The results are not difficult to understand if one is familiar with the work of A. Coca [13a] and R. Kohn.[13b]

The tendency for nummular eczema to eventually "burn itself out" we relate to the spontaneous desensitization and immunization which comes after harboring staphylococci for long periods. The "burning out" process usually requires years. The administration of Staphylococcus vaccine-toxoid can accomplish the same result in months.

Although cutting oil and certain other oils are known to be incitants of pustular processes, we found that in our series the incidence of patients who were mechanics was not significantly large. The area from which our patients come is, however, largely rural. It is our impression that eczema in the mechanics we treated was more difficult than the average to control, and that mechanics were more likely to have persistent recurrent plaques on the dorsal surfaces of the digits, especially over the joints.

13. Swineford, O., Jr., and Holman, J.: Studies in Bacterial Allergy: Results of 3860 Cutaneous Tests with 34 Crude Polysaccharide or Nucleoprotein Fractions of 14 Different Bacteria, J. Allergy **20**:420 (Nov.) 1949.

13a. Coca, A. F.: Familial Nonreaginic Food-Allergy, Springfield, Ill., Charles C Thomas, Publisher, 1943.

13b. Kahn, R. L.: Tissue Immunity, Springfield, Ill., Charles C Thomas, Publisher, 1936.

Housewives made up the largest occupational group of our patients with nummular eczema. The average housewife has her hands in water at least one and a half hours per day, which is six times more than that of the average man. We believe that the moisture, which creates favorable growth conditions for the staphylococci, is of greater importance than the action of soap. Portals of entry for bacterial invasion may be created by minor cuts and abrasions obtained while washing knives and kitchen utensils, in the use of steel wool and abrasives, and in minor burns sustained in handling hot utensils.

In our series, clinical evidence of vitamin A deficiency was noted only a few times. The administration of vitamin A under controlled conditions in those patients who had no evidence of vitamin A deficiency produced no improvement. Paul Gross,[14] who advocated the use of vitamin A in nummular eczema also, used tar ointment, which is still one of the best therapeutic agents for the treatment of this disease. We suspect that if he had given vitamin A alone without this excellent remedy, there would have been no significant improvement in his patients. We believe that the lack of folic acid and the vitamin B complex is often more important than the lack of vitamin A.

We feel that if careful attention is given to nutrition, bacterial allergy, and the use of selective culture media for the quantitative estimation of surface streptococci and staphylococci, it will be possible to evaluate and to treat nummular eczema and other eczematous eruptions with more certainty and precision than has been possible in the past.

CONCLUSIONS

1. Staphylococci play a major role in the etiology of nummular eczema.

2. The pigmented and mannitol-fermentive forms of staphylococci are significantly numerous in the plaques of nummular eczema.

3. Nummular eczema, as a disease entity, can be satisfactorily explained by the triad of etiological components, namely, (1) poor nutrition, (2) bacterial allergy to the allergens of the staphylococci, and (3) bacterial invasion of the skin by the Staphylococcus.

4. In dermatitis venenata or allergic eczematous contact-type dermatitis, staphylococci are no more numerous on the eczematous skin during the first few days of the acute attack than on the normal skin.

5. Mannitol salt agar (Difco) is an excellent selective medium when used in contact plates as described for the quantitative estimation of the surface staphylococci on the skin.

14. Gross, P.: Nummular Eczema: Its Clinical Picture and Successful Therapy, Arch. Dermat. & Syph. **44**:1060 (Dec.) 1941.

Clinical Notes, New Instruments and Techniques

USE OF HEPARIN IN TREATMENT OF PSORIASIS

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In the hope of stimulating further studies in a more extensive and a more nearly exact manner than is possible to me, I wish to make this short preliminary report on the use of heparin [1] in the treatment of psoriasis.

Only three cases are included in this report, but these cases were especially interesting because the patients did not respond well to ordinary methods of treatment or else did not tolerate them well. Heparin was merely added to the program in addition to whatever else was being used at the time, when progress was definitely at a standstill and the condition was not satisfactory. Other patients have been treated with this method, with indeterminate results up to now; their cases are not yet ready to be reported.

REPORT OF CASES

CASE 1.—Mrs. J. H. McN., a white woman, aged 64, had had recurrent attacks of contact dermatitis for years, but it was not until 1951 that a definite psoriasis developed. She did not tolerate mercury or salicylic acid. At one time, when the psoriatic eruption was intermingled with eczematoid dermatitis she had received benefit from cortisone. Lipotropic substances were administered (Methischol [*dl*-methionine, choline, inositol, together with the natural B complex from liver]), but there was no definite improvement. Vitamin B_{12} by mouth and ultraviolet irradiation did not bring about improvement.

On May 8, 1952, the coagulation time being normal, treatment was begun with aqueous heparin sodium, 50 mg. three times a week. Later vitamin B_{12} was administered by injection, along with the heparin, in doses of 50 γ. After heparin had been used for about a month, slow improvement was noted. Later, the number of injections was reduced to two each week. Gradual improvement has continued and the over-all improvement may be classified as moderately good, all areas having cleared except for a few of the recalcitrant patches in the usual areas of psoriasis.

CASE 2.—D. J., a white woman, aged 35 years, has had psoriasis for 12 years. The skin condition became much worse immediately after bilateral oophorectomy eight years ago. The usual topical remedies had been employed, with little success, and the patient had been without any treatment at all for some time before the present program was instituted.

The coagulation time being normal, the first injection of repository heparin (Depo-Heparin) was administered on Sept. 10, 1952, in a dose of 100 mg. Subsequent injections were in doses of 200 mg. The coagulation time was checked before each of the first four injections and remained within normal limits. For three weeks the injections were administered twice a week; after that they were administered once a week.

Local treatment consisted of 10% coal tar solution in Nivea oil for the body and Mercreol (½% oleate of mercury and ¾% cresol in a pectin and mineral oil base [Texas Pharmacal Company]) for the scalp.

Aqueous heparin sodium was furnished for these studies by The Upjohn Company and the Abbott Laboratories, and repository heparin (Depo- Heparin) was furnished by The Upjohn Company.

1. (*a*) Grütz, O., and Burger, M.: Die Psoriasis als Stoffwechsel problem, Klin. Wchnschr. **12**:373-379 (March 11) 1933. (*b*) Gross, P., and Kesten, B. M.: The treatment of Psoriasis as a Disturbance of Lipid Metabolism: Further Observations on Lipotropic Therapy Based on a 10-Year Clinical Study, New York J. Med. **50**:2683-2686 (Nov. 15) 1950.

Improvement was noted in two weeks and became pronounced soon after that, continuing at a rather rapid rate for about three months, and then tapering off. At present, after 19 injections there is still moderately marked scale in the scalp and scattered areas of mild psoriatic eruption on the trunk and extremities, but there is a marked over-all improvement.

CASE 3.—I. S., a white woman aged 28, has had psoriasis since early childhood. She had been treated by prominent dermatologists in various parts of the country. She tolerates sunlight very poorly and shows some degree of irritation from applications of mercury and crude coal tar. Her recent treatment has included the use of these substances up to the limit of tolerance. Internally many agents were employed. Lipotropic therapy was instituted with Methischol. Small doses of *d*-amphetamine (Dexedrine) sulfate were given. For a period of several months, the condition improved while cortisone and corticotrophin (ACTH) were administered. Then, even while the administration of these hormones was continued, the condition relapsed. For its lipotropic effect as well as for its general tonic effect, vitamin B_{12} was given both by mouth and by injection, and for some six months the condition was moderately improved. Then again the condition became much worse, even while the patient was receiving vitamin B_{12} and Methischol in rather large doses.

On Oct. 6, 1952, with suitable precautions, treatment with heparin (Depo-Heparin) was begun; 200 mg. was given once a week except for several interruptions caused by events over which the patient had no control. All other forms of treatment were continued without change. Improvement was noted within two weeks, and after eight injections of heparin the condition was greatly improved, although the eruption had not cleared entirely.

COMMENT

The idea of using heparin in the treatment of psoriasis stems from combining the older theories of the etiology of psoriasis as a disturbance of fat metabolism with some new observations made by Gofman and his co-workers.

That psoriasis is associated with a faulty fat metabolism is a theory held by a number of dermatologists.[1] Quantitative studies on the total lipids in the blood, or on cholesterol, or cholesterol ester levels have given conflicting results.[2] Therefore the idea is entertained that the disorder may be qualitative as well as quantitative basically.

A new method of qualitative fractionation of the serum lipoproteins was outlined by Gofman and his associates.[3] By means of the ultracentrifuge they determined the presence in the serum of lipoprotein molecules of different sizes and were able to settle on a certain lipoprotein spectrum which seemed to be the normal one.

Furthermore, Gofman and his co-workers found that certain diseases were associated with fairly definite and constant alterations in the lipoprotein spectrum.[4] In atherosclerosis and myocardial infarction, for instance, they found a relative increase in the Sf_{10-20} molecules. Xanthomatous diseases showed a similar picture.[5]

Further studies indicated that heparin is a substance which, when injected into the patient, produces a tendency for the abnormal lipoprotein spectrum to become normal.[6] This effect has

2. Gross,[1b] Madden, J. F.: Cholesterol Balance and Low Fat Diet in Psoriasis, Arch. Dermat. & Syph. **39**:268-277 (Feb.) 1939.

3. Gofman, J. W.; Lindgren, F. T., and Elliott, H.: Ultracentrifugal Studies of Lipoproteins of Human Serum, J. Biol. Chem. **179**:973-979 (June) 1949.

4. Gofman, J. W.; Lindgren, F. T.; Elliott, H.; Mantz, W.; Hewitt, J.; Strisower, B.; Herring, V., and Lyon, T. P.: The Role of Lipids and Lipoproteins in Atherosclerosis, Science **111**:166-171 (Feb. 17) 1950.

5. Epstein, N. N.; Rosenman, R. H., and Gofman, J. W.: Serum Lipoproteins, and Cholesterol Metabolism in Xanthelasma, A. M. A. Arch. Dermat & Syph. **65**:70-81 (Jan.) 1952.

6. Graham, D. M.; Lyon, T. P.; Gofman, J. W.; Jones, H. B.; Yankley, A.; Simonton, J., and White, S.: Blood Lipids and Human Atherosclerosis: The Influence of Heparin upon Lipoprotein Metabolism, Circulation **4**:666-673 (Nov.) 1951.

been used with some success in the treatment of coronary sclerosis and xanthomatosis. Stewart, Clark, Dragstedt, and Becker approached the psoriasis problem from a somewhat similar point of view when they used lipocaic as a method of treatment.[7]

Although N. Epstein states[8] that abnormalities in the lipoprotein spectrum in psoriasis have not been detected by means of the ultracentrifuge, the possibility was nevertheless considered that heparin might act in some unknown manner to produce normal qualitative and quantitative conditions in the lipids of the body. With these thoughts in mind and with suitable precautions, heparin was administered to these patients.

Vitamin B_{12} was part of the treatment in some of these patients. The use of this lipotropic substance as an adjunct in the treatment of psoriasis seems to hold some promise, but that subject necessarily will not be a part of this report.

CONCLUSIONS

In the hope of bringing the fat metabolism to a more nearly normal state, heparin was used as a part of the treatment in patients with psoriasis. The cases of three patients who seemed to be benefitted by such treatment are reported here.

This method is not put forth as a cure for psoriasis, but is believed to show some promise as an adjunct in the treatment of this chronic disease.

A repository type of heparin, administered not more often than once a week, seemed to be better than aqueous heparin in smaller doses more frequently.

It is hoped that the observations recorded here may lead to more study along the same lines, with, possibly, greater benefits to the victims of this obstinate disease.

SUMMARY

A report is made on the use of heparin in the treatment of psoriasis. Three case reports are presented which seem to indicate that some benefit may be derived from this form of treatment.

7. Stewart, C. D.; Clark, D. E.; Dragstedt, L. R., and Becker, S. W.: The Experimental Use of Lipocaic in the Treatment of Psoriasis: Preliminary Report, J. Invest. Dermat. **2**:219-230 (Aug.) 1939.

8. Epstein, N.: Personal communication to the author.

DERMATITIS DUE TO DERMANYSSUS GALLINAE OF PIGEONS

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CINCINNATI

It is not well known that the mite, Dermanyssus gallinae, may infest pigeons. Three cases of dermatitis due to D. gallinae infestation of pigeon are being reported, as this source may be overlooked when tracing the etiology of lichen urticatus suspected to be a reaction to the bites of arthropods.

Three white women who share an apartment were seen in May, 1952, with malaise and a pruritic papular eruption on the extremities, neck, and around the waist. History revealed that pigeons roosted outside one window, and many small arthropods were found on the window sill and inside the screen. These were identified as D. gallinae by C. F. Muesebeck and W. C. McDuffie, of the Bureau of Entomology and Plant Quarantine of the United States Department of Agriculture. The mites are especially apt to enter the living quarters after young birds have left the nest. Area control was accomplished in this instance with the repeated painting of D.D.T. (1,1,1-trichloro-2,2-bis [*p*-chlorophenyl]ethane) in a varnish base on the window sill and screen. The dermatitis and symptoms subsided within a week.

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NEW ANTIBACTERIAL DETERGENT FOR COMMON SKIN DISEASES IN CHILDREN

Use in Prophylaxis and Treatment

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In the summer of 1951, while we were on pediatric service at an affiliate children's hospital and infant home, we were impressed with the prevalence of skin disorders, such as urticaria, impetigo, diaper rash, secondary infection occurring after insect bites, and heat rash among children. It seemed that an agent which would reduced the incidence of these conditions and yet not sensitize or irritate the skin might be of value. A new antibacterial detergent [1] was considered to be worthy of clinical investigation.

Interest was aroused in this product because of its reported cleansing and antibacterial properties [2] and because of the published reports of the antibacterial properties of pHisoHex (Winthrop-Stearns),[3] a similar antibacterial synthetic detergent containing 3% of hexachlorophene on a total weight basis, used as surgical "prep" by surgeons and nurses.

PURPOSE

The purpose of this study was to determine whether a soapless antibacterial cleansing agent used routinely could (1) clear superficial skin lesions common to children confined to a hospital or an institution for a long period of time, where individual care is limited, and (2) prevent recurrence of such eruptions.

METHOD OF CONDUCTING THE STUDY

The study was conducted in a children's hospital and infant home housing about 400 children ranging in age from the newborn infant to children 5 years old. One hundred twenty-five children between the ages of 3 weeks and 5 years were washed daily with the preparation, the detergent being used in the same manner as soap. The regimen consisted of daily over-all

Dr. Carl Fisher, head of the Division of Pediatrics, Hahnemann Medical College and Hospital, gave cooperation and guidance.

From the Division of Pediatrics, Hahnemann Medical College and Hospital, and St. Vincent's Hospital for Women and Children.

1. The detergent used in the study was Tod'l, manufactured and supplied by the Centaur-Caldwell Division of Sterling Drugs, Inc. This product is an emulsion composed of a sulfonated ether, petrolatum, and wool fat cholesterols. It contains hexachlorophene, 0.5%, which is a bactericidal synthetic diphenol with the chemical formula bis-(2-hydroxy-3,5,6-trichlorophenyl) methane.

2. Dennis, E. W.: Unpublished data in the files of Sterling-Winthrop Research Institute.

3. Walter, C. W.: The Aseptic Treatment of Wounds, New York, The Macmillan Company, 1948. Fine, J.: The Care of the Surgical Patient, Philadelphia, W. B. Saunders Company, 1949. Thirlby, R. L., and Nesbit, R. M.: Clinical Evaluation of a Bactericidal Detergent for Hand Preparation in Urologic Practice, J. Urol. **62**:617 (Oct.) 1949. Bowers, R. F.: pHisoderm with Hexachlorophene (G-11): Its Integrity as a Surgical Scrub, Am. J. Surg. **78**:859 (Dec.) 1949. Chisholm, T. C.; Duncan, T. L.; Hufnagel, C. A., and Walter, C. W.: Disinfecting Action of pHisoderm Containing 3 Per Cent Hexachlorophene on the Skin of the Hands, Surgery **28**:812 (Nov) 1950. Freeman, B. S., and Young, T. K., Jr.: Use of a Detergent (pHisoderm®) Combined with Hexachlorophene for Skin Disinfection, Arch. Surg. **61**: 1145 (Dec.) 1950. Artz, C. P.; Pulaski, E. J., and Shaeffer, J. R.: Clinical Uses of Hexachlorophene, U. S. Armed Forces M. J. **2**:819 (May) 1951. Dull, J. A.; Zintel, H. A.; Ellis, H. L., and Nichols, A.: An Evaluation of pHisoderm G-11 and a Liquid Soap Containing G-11 When Used as the Preoperative Scrub, Surg, Gynec. & Obst. **91**:100 (July) 1950.

cleansing of the hair, face, and body, as well as the application of the preparation to the groin and buttocks following change of diapers. No soap, lotion, cream, oil, or powder was used at any time.

The study of this group was controlled by using 115 other infants and children in the same age group who initially presented normal skins and who were bathed with a common soap. Each child was observed daily and the skin status noted.

The children included in our test series presented healthy skins, insect-bitten skins with and without secondary infection, intertrigo, diaper rash, impetigo, eczema, miliaria, allergic dermatitis, and chicken pox. Those who had no skin eruptions were tabulated for continuance of the normal state of the skin, but our emphasis was placed on those with abnormal skin manifestations.

BACTERIOLOGIC PROPERTIES

The bacteriologic properties of the preparation were compared by Dennis [2] with the bacteriologic properties of hexalchlorophene (pHisoHex), using the agar contact plate method. The results of these tests suggested that this preparation compared favorably with hexachlorophene (pHisoHex) with respect to degerming of the skin.

TABLE 1.—*Comparison of Children Bathed with the Soapless Detergent Vs. Children Bathed with Soap*

Treatment	Patients, No.	Condition of Skin		Results		
		At Start	Developed During	Cleared	No Change	Made Worse
Detergent	41	Clear	.....	..	41*	0
Soap	115	Clear	.....	..	65*	50
Detergent	40	Diaper rash	.....	40	0	0
Soap	35	Clear	Diaper rash	7	28†	0
Detergent	5	Miliaria	.....	5	0	0
Soap	15	Clear	Miliaria	0	15††	0

* By "No Change" is meant maintenance of normal skin.
† Skin cleared temporarily, but diaper rash recurred.
†† Miliaria cleared coincident with onset of cool weather.

RESULTS

At the end of three months' continued observation, 95 children, or 76% of those children having skin disorders, presented marked clearing, one case of eczema was not benefited, while 29 children, or 23%, showed complete clearing after the use of the detergent.

The skin of the children in the group which used the antibacterial synthetic detergent was cleaner, softer, and free of blotchy erythema, as compared with the skin of those who had been bathed with soap.

In the control (soap) group superficial infections persisted for longer periods; the skin was dry, rough, and much more easily traumatized by wet diapers and soiled linen.

A comparison of the two groups is presented in Table 1. It will be noted that no change was observed in the 41 children with normal skin who were bathed with the soapless detergent. Their skin remained clear and soft throughout the trial period. In contrast to this, of the 115 children in the soap group, skin eruptions developed in 50 children (35 cases of diaper rash, 15 cases of miliaria). Although the other 65 children who were bathed with soap are recorded as having evidenced no change in the appearance of their skins, it was our clinical impression that in reality their skins were drier and rougher than those of the children bathed with the soapless detergent.

In Table 2 the mean clearing times for the detergent-treated group and the soap-treated group are compared. The detergent appeared to effect a more rapid improvement, and no recurrences or skin irritation were noted. Not only did the skin of the children who were bathed with soap take longer to clear, but a large percentage (80%) of the diaper rashes reappeared.

In order to observe the effect of the soapless detergent on as many other types of skin eruptions as possible, 39 children who presented a variety of conditions were washed with it. The results of this phase of the study are shown in Table 3.

Most of the nurses who used the preparation were enthusiastic about it. They reported that the skin of the children was clearer, of finer texture, and much easier to keep clean. Most nurses commented on the fact that the incidence of skin disorders seemed to be much less than in previous years. None of the nurses complained that the detergent irritated their own hands. In fact, the skin of some was reported as being better after they had used the soapless detergent for a few weeks.

TABLE 2.—*Comparison of Mean Clearing Times of Diaper Rash and Miliaria*

Condition	Detergent			Soap		
	Cases, No.	Mean Clearing Time	No. of Cases Recurring	Cases, No.	Mean Clearing Time	No. of Cases Recurring
Diaper rash (severe) *	6	10	0	None	..	..
Diaper rash (moderately severe)	34	6	0	23	10	28 (80%)
Diaper rash (mild)	0	..	..	12	6	
Miliaria	5	6	0	15	No effect †	..

* Severe diaper rash was treated only with the detergent to subject it to as rigorous a trial as possible, as possible.

† Skin cleared coincident with cool weather.

TABLE 3.—*Use of the Soapless Detergent in Miscellaneous Skin Eruptions*

Condition	Cases, No.	Observations
Insect bites		
Without secondary infection	14	Cleared in 4 to 8 days
With secondary infection	2	Cleared in 5 to 16 days
Rough skin	5	Skin became softer and clearer within 10 days
Furunculosis	4	Cleared in 11 days
Herpes labialis	3	Cleared in 7 days
Varicella	3	One moderately severe case cleared in 11 days, 2 mild cases cleared in 5½ days. It was our observation that less pruritus, scaling and crusting occurred
Generalized excoriation from bed linens	2	Cleared in 11½ days
Eczema	1	No effect noted
Papular urticaria	1	Improved in 6 days; cleared within 10 days
Tinea capitis	1	Appeared to suppress further scalp infection during 2 months' observation
Seborrhea	1	Improvement in 4 days, but remained stationary thereafter
Generalized impetigo	1	Improved in 2 weeks; cleared within 5 weeks
Impetigo of head	1	Cleared within 10 days

SUMMARY AND CONCLUSIONS

A synthetic, sudsing, antibacterial detergent [1] appeared effective in clearing and preventing common skin disorders in children exposed to long periods of hospitalization or institutional care.

Many cases of miliaria, diaper rash, and impetigo were cured in periods varying from one week to three months. In former years similar conditions had been reported as having persisted for much longer periods.

The detergent was effective in reducing the recurrence of skin irritation commonly observed in infants and children in prolonged contact with beddings and linens.

No irritation or allergic sensitivity of the skin was noted from the use of this preparation.

The detergent reduced the necessity of bathing the infants and children more than once a day.

GRANULAR CELL MYOBLASTOMA

Report of a Case

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Striated muscle cell tumors, depending upon the type of cells from which they are derived, are classified as rhabdomyomas and myoblastomas. Rhabdomyomas are tumors derived from mature striated muscle cells, whereas myoblastomas are derived from juvenile muscle cells, or embryonic myoblasts. Abrikossoff,[1] in 1926, initially described the latter tumor under the title of myoblastic myoma; it has since been referred to as myoblastoma, granular cell rhabdomyoma, and granular cell myoblastoma. Abrikossoff originally believed that the tumor cells were derived from muscle fibers undergoing changes occurring after injury. Later, he concluded that they arose from embryonal striated muscle cells. Over 200 cases have been described since the original report. Lesions are located most frequently in the upper digestive and respiratory tracts. Cutaneous lesions comprise approximately 20% of the recorded cases, being second in frequency only to lesions of the tongue. Not many of the recorded cases have been published in dermatologic literature.[2] The tumors do not resemble leiomyoma clinically nor histologically.

DESCRIPTION

Cutaneous myoblastoma is usually a solitary firm symptomless lesion varying from a few millimeters to several centimeters in diameter. There is reputedly nothing characteristic in their appearance. The clinical features in our patient strongly resemble those of a case recently reported by Kern, Kaufman and Combes.[2b] Sessile and pedunculated tumors have been recorded. Gradual increase in size and eventual ulceration is not infrequent in lesions of long duration. The highest age incidence is in the third, fourth and fifth decades. Myoblastoma is generally considered benign, and wide local excision is adequate treatment. It does not tend to recur after complete excision. In rare instances, the tumor has proved to be malignant.[3]

HISTOLOGIC ASPECTS

Myoblastoma consists of large irregular polygonal cells. The cytoplasm is coarsely granular and often acidophilic. The nuclei are small and spherical; some cells may be multinucleated. Although they resemble xanthoma cells, special staining does not show the presence of lipids. The cells are generally located in variously-sized groups throughout the corium. A few observers have described longitudinal and cross striations suggestive of myofibrils in the granular cells of some tumors.[4] Pseudoepitheliomatous hyperplasia of the skin or mucous membrane overlaying

* From the Department of Medicine (Dermatology), New York Hospital and Cornell University Medical College.

1. Abrikossoff, A. I.: Ueber Myome ausgehend von der quergestreiften willkürlichen Muskulatur, Virchows Arch. path. Anat. **260**:215, 1926.

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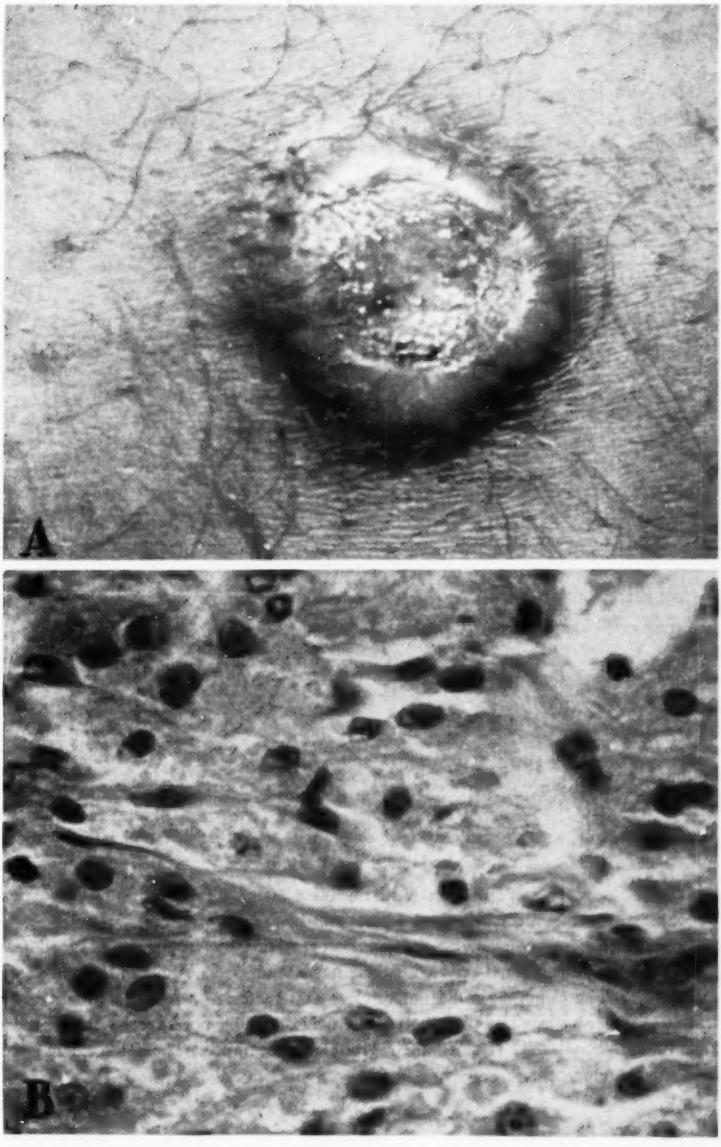

Cutaneous myoblastoma: *A*, granulomatous lesion with central ulceration and smooth rolled border (3.3 cm. in diameter); *B*, microphotograph demonstrating the characteristic clusters of large polygonal cells, with coarsely granular acidophilic cytoplasm and rounded nuclei.

the myoblastoma cells may be present. Some regard the polygonal cells as being derived from embryonal muscle cells, whereas others maintain that they develop from muscle fibers undergoing necrobiotic changes or granular degeneration from injury.[5] The former theory is the one that is generally accepted.

CASE REPORT

A 28-year-old white man was initially seen in the dermatology clinic of New York Hospital on Aug. 7, 1950. His chief complaint was of gradually enlarging symptomless lesion of seven months' duration on his right thigh. His past history was noncontributory, and he said that there was no prior venereal disease. The patient first noted a "pimple" on his thigh in January, 1950. This gradually progressed in size, becoming ulcerated in July. His general health was not affected. No preexisting lesion was known to have been present in the affected region, and history of trauma to the involved area could not be elicited. No correlation could be determined between his occupation and the lesion. He had received no treatment for the tumor prior to his visit to New York Hospital.

The results of the physical examination were essentially negative, except for the right thigh, where a cutaneous lesion was present in the midline on the anterior aspect in the proximal third. There was no femoral or inguinal lymphadenopathy. The tumor was circinate, with a diameter of 3.3 cm. It consisted of a central ulceration 2.2 cm. in diameter, surrounded by a cord-like rolled smooth reddish border 3 mm. in width; this, in turn, was enclosed within a zone of purplish hyperpigmentation 2.5 mm. in width. The ulcerative portion had a fine granulomatous base and was covered with a yellowish crust. There was no purulent material present. The entire lesion was well demarcated, indurated, and, when tested by palpation, apparently extended fairly deep. The patient's temperature was normal, and his blood pressure was 142/90. A definite clinical diagnosis was not made. Some of the clinical features suggested basal-cell epithelioma, Bowen's disease, lymphosarcoma, tumor *d'emblée* of mycosis fungoides, diphtheria ulcer, deep mycotic infection, and granuloma inguinale were also considered.

The erythrocyte count was 4,700,000; the hemoglobin content was 14.5 gm. per 100 cc., and the thrombocyte count was within normal limits. The leucocyte count was 11,800, with a differential distribution of 66% neutrophiles and 34% lymphocytes. Blood cholesterol and serum proteins were within normal range. Serologic reactions for syphilis were negative, the urinalysis showed normal results, and smears for Donovan bodies gave negative results. Cultural examinations for fungi and bacteria on Löffler's medium and on Sabouraud's medium, as well as on aerobic and anaerobic media, gave negative results. A tuberculin skin test (old tuberculin 1:25,000) showed a positive reaction.

The lesion was surgically excised by elliptical incision, in order to include a wide margin of normal tissue. Examination one year later did not disclose any indication of recurrence.

The histologic sections were diagnostic of myeblastoma. The epidermis exhibited moderate regular acanthosis, except in the region of ulceration. In the dermis were small clusters of large polygonal cells with coarsely granular acidophilic cytoplasm and rounded nuclei. There were no mitotic figures. The polygonal cells with their nuclei and granules assumed a pink color with the Masson stain. The Gram stain did not disclose any bacteria or fungi in the areas occupied by the large granular cells. The phosphotungstic acid stain did not reveal any striated muscle fibers, and the polygonal cells retained their granular appearance. The fat stain did not show any lipids in the tumor cells.

SUMMARY

The clinical features and histologic findings of a case of myoblastoma are reported. There has been no recurrence after the surgical excision one year ago.

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66 East 66th St.

TOXIC PSYCHOSIS FOLLOWING USE OF STILBAMIDINE IN BLASTOMYCOSIS

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AND
R. JACKSON, M.D.
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After the report of Schoenbach [1] on the use of stilbamidine in tretatment of blastomycosis, this form of treatment was tried in a case of widespread blastomycosis. The case is being reported, first, to show the efficacy of the drug in this infection and, second, to draw attention to a possible severe toxic reaction to the drug.

REPORT OF A CASE

Miss B. G., aged 40, was first seen in the outpatient department of the Montreal General Hospital on Aug. 28, 1952, at which time she gave the following history: She had lived all her life in Canada, in rural areas. While she was in high school she had had a bad fall, injuring her head, and six months later alopecia totalis developed. When she was 26 years old, asthma developed after a severe upper respiratory infection; the asthma has persisted to the present. She had pneumonia with pleurisy in 1942. In July, 1949, she spent a month at a nursing home in the southeastern part of Quebec and was in the fields much of the time. In October, 1949, a small "boil" developed on one of her fingers. This was treated by herself and her family doctor. The "boils" spread, and in November, 1951, she consulted a dermatologist, who diagnosed blastomycosis and treated her with potassium iodide and aureomycin, with some improvement.

At the time of her first visit, she showed extensive heaped-up granulomatous lesions on her forehead, cheeks, forearms, and legs.

On investigation two cultures were positive for Blastomyces dermatitidis, a skin test with blastomycin was positive, a biopsy showed chronic suppurative dermatitis compatible with blastomycosis, and a chest x-ray showed minimal left lower lobe parenchymal disease compatible with long-standing asthma. Pending her hospital admission, iodides and sulfisoxazole (Gantrisin) were prescribed, with little change. Finally, after much persuasion, she was admitted to the hospital on Oct. 30, 1952.

On admission, her weight was 70 lb. (31.5 kg.) and her height 4 ft. 11 in. (150 cm.). She gave a history of amenorrhea for one year. Abnormal laboratory findings prior to the use of stilbamidine were the following: coagulation time, 18 minutes; prothrombin time, 32 seconds; total serum protein, 6.38 gm. per 100 cc. (albumin 2.94 gm., and globulin 3.44 gm.); blood urea nitrogen 25 mg. per 100 cc., and cephalin-cholesterol flocculation 3 +. The complement-fixation test for Blastomyces was negative.

A freshly prepared solution of stilbamidine was given intravenously with 100 cc. of 5% dextrose by the following dosage schedule: Nov. 1, 50 mg.; Nov. 3, 100 mg., and Nov. 5 to 12 inclusive, 150 mg. daily. The total dose was 1.35 gm. over 12 days. The skin lesions reacted dramatically. First, the granulomatous picture disappeared, leaving a dry crusted lesion. Later the crusts dropped off, leaving a clean base.

On Nov. 13, 1952, the patient became suddenly disorientated as to time and place and marked paranoid trends developed. She was sedated. The psychiatric consultant diagnosed this condition as "toxic psychosis."

The laboratory findings following administration of stilbamidine were albuminuria, total protein 7.05 gm. (albumin 3.07 gm. and globulin 3.98 gm.), blood urea nitrogen 13 mg. per 100 cc., and cephalin-cholesterol flocculation 3 +.

From the Department of Dermatology, Montreal General Hospital.

1. Schoenbach, E. B.; Miller, J. M., and Long, P. H.: The Treatment of Systemic Blastomycosis with Stilbamidine, Ann. Int. Med. **37**:31-48 (July) 1952.

As this patient had been very apprehensive about hospitalization and as she resisted much of the investigation, it was felt that a considerable portion of her mental upset was on this basis. As soon as her mental condition began to improve, she was discharged home, on Nov. 17, in an attempt to reduce her anxiety.

She suffered a severe mental relapse at home and was certified for admission to a mental institution. However, before she could be admitted there, she required medical care for a fever which began shortly after her discharge from hospital. She was readmitted to the Montreal General Hospital on Nov. 21.

On the second admission the patient was about the same physically, except for an almost continuous temperature of 101 F. Mentally, she was not acutely ill, but she was far from being in touch with reality. The fever continued, and on Dec. 9 a diagnosis of staphylococcal pneumonia was made. Her urine on two occasions showed albumin. The plasma protein, red blood cell count, and hemoglobin declined steadily. The cephalin-cholesterol flocculation remained 3+. Results of other investigations were essentially normal. The psychiatric consultant on Dec. 17, 1952, reported: "The patient today is in perfect touch with reality. The acute psychiatric problem has solved itself. There remains the chronic—indeed lifetime—problem of a cloistered neurotic personality." She was treated with chloramphenicol (Chloromycetin) and blood transfusions and appeared to be improving. Her skin by this time was almost clear. She died in her sleep on Dec. 30. Unfortunately, permission for a postmortem examination was not obtained.

COMMENT

A case of widespread cutaneous blastomycosis is presented. There is some suggestion of internal involvement, but this has not been proved. While the cutaneous lesion responded well to intravenously administered stilbamidine, it would appear that this drug was, at least in part, responsible for the development of her psychiatric state. As is frequently the case in toxic psychoses, many underlying factors were present in the case. The patient had lived a cloistered life because of her alopecia totalis and her widespread skin disease and was suddenly thrust into a public ward, where she was the object of much interest and attention. The relative importance of these factors is impossible to evaluate. To our knowledge, no such toxic reactions have been reported heretofore, and for this reason we wish to report this case. It is most probable that this woman received too large a dose of stilbamidine for her weight. We do not know whether the therapy contributed to her death.

SUMMARY

A case of cutaneous blastomycosis is reported. The patient showed dramatic improvement while receiving stilbamidine, but a severe toxic psychosis developed during the course of therapy.

1414 Drummond St.

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

James R. Webster, M.D., *President*

Irene Neuhauser, M.D., *Secretary*

Oct. 15, 1952

Keratoma Hereditarium Dissipatum Palmare et Plantare with Cutaneous Horn Formation (Brauer) Treated with Lithium Bromide. Presented by (by invitation) Dr. Allan L. Lorincz.

Mrs. H. A., a housewife aged 49, came to the University of Chicago Clinics in August, 1952, complaining of painful horny growths on both feet for the past 25 years. Her mother, maternal aunt, four brothers, and three sisters all have had a similar disorder. Some of the mother's grandchildren also have such lesions. Most of the afflicted siblings have, in addition, had "polyneuritis," but details of this are not available.

Results of physical examination, except for the skin lesions, were essentially normal, as were results of routine blood cell counts, urinalysis, and chest X-ray.

The plantar and palmar skin showed sharply localized hyperkeratotic lesions, many of which were simply small horny papules, but others on the feet were very hard fissured tender horn-like growths, 1 cm. or more in diameter, which protrude as far as 1 cm. beyond the skin surface. These greatly interfered with walking. There is no history of arsenic intake.

For the past six weeks 17% lithium bromide in nail lacquer has been applied daily to the largest horny lesions. This treatment has successfully softened and removed the most troublesome horny portions of these lesions.

Histologic sections are not available.

DISCUSSION

Dr. Adolph Rostenberg Jr.: I want to ask about the absorption of the lithium. A few years ago lithium was used as a substitute for salt. It was taken off the market because there were several deaths after its use. I do not know whether it is absorbed by the skin.

Dr. Stephen Rothman: We studied the literature on toxicity of lithium salts and found that they are toxic only when sodium is withdrawn. Anyhow, our own experiments revealed that the percutaneous absorption of lithium is minimal.

Dr. Allan L. Lorincz: The rationale for the use of lithium bromide in the case reported is based on the work of P. Alexander, who first studied the effect of concentrated lithium bromide solutions on wool fibers and noted a pronounced loosening effect on this type of hard keratin structure. This keratin loosening effect was explained by the hydrogen-bond disrupting effect of concentrated lithium ion solutions. The small strongly electropositive lithium ions in aqueous solution are ordinarily surrounded by thick hydration shells of many water molecules. In concentrated solutions not enough water is available to fully hydrate all the lithium ions, so that the electronegative groups of keratin, such as NH and OH, which ordinarily partake in hydrogen bonding, are drawn instead into the orbits of the lithium ions.

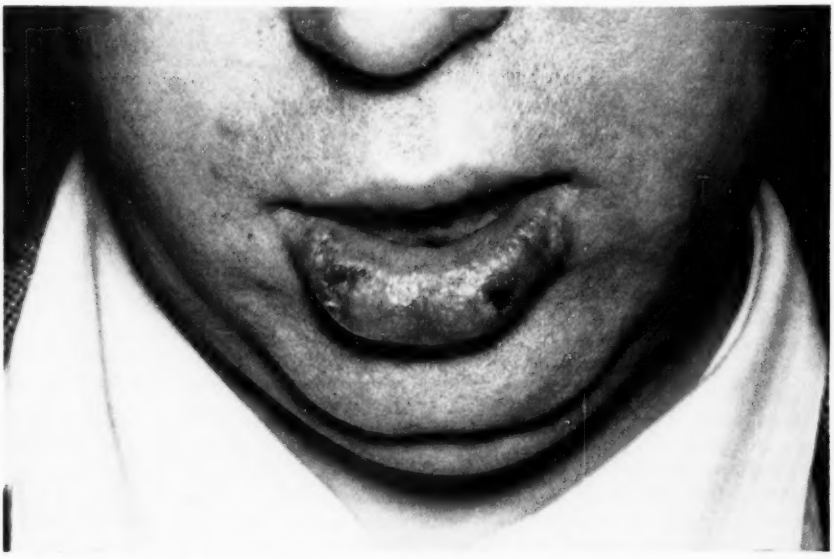
This hard keratin loosening effect of lithium bromide was rather successfully applied in this case to soften and thus to remove the troublesome cutaneous horns.

Dr. Rothman: To Dr. Lorincz' explanation I should like to add that in contrast to all other keratolytic agents lithium bromide does not break the disulfide linkages or other covalent chemical bonds in keratin, but breaks the hydrogen bonds only. This leads to a reversible loosening of the keratin molecule. We have utilized this effect in increasing the permeability of hair (*J. Invest. Dermat.* **17**:9, 1951) and in the treatment of onychomycosis (A. M. A. Arch. Dermat. & Syph., **67**:239, 1953).

Chronic Discoid Lupus Erythematosis Treated with Quinacrine Hydrochloride (Atabrine Dihydrochloride). Presented (by invitation) by DR. GEORGE C. WELLS.

R. B., a housewife aged 32, has had chronic discoid lupus erythematosis of the face, scalp, and buccal mucosa for four years. Itching and soreness in the lesions have been troublesome. She has been treated with bismuth, gold, oxophenarsine hydrochloride (Mapharsen), quinine, vitamin B_{12}, and vitamin E, without improvement. In August, 1952, the lesion between the eyebrows was infiltrated with 17-hydroxycorticosterone (Compound F). On two occasions 25 mg. of hydrocortisone were injected and on one occasion 75 mg. The lesion became paler and markedly depressed; however, this treatment was discontinued owing to the danger of ugly scarring.

In June, 1952, quinacrine hydrochloride (Atabrine dihydrochloride), 0.2 gm. daily, was given and steady improvement took place over two months, after which time the dose was lowered to 0.1 gm. daily. Besides paling of the lesions and diminution of scaling, the itching and soreness were relieved.



Photograph taken Aug. 18, 1952, before the start of quinacrine therapy. There are silvery scaling and erosion of the lower lip, together with marked swellings. Red raised patches extend to the skin beyond the lip margins.

At present, resolution is incomplete, but she is much better than at any time during the last four years. There is general yellow staining of the skin.

On general examination there has been no evidence of systemic disease. Blood cell counts, urinalysis, serological tests, and sedimentation rate have shown normal results.

Chronic Discoid Lupus Erythematosis Treated with Quinacrine Hydrochloride (Atabrine Dihydrochloride). Presented by (by invitation) DR. GEORGE C. WELLS.

L. F., a store owner aged 42, has had chronic discoid lupus erythematosis for 11 years. Eyelids, face, lips, and buccal mucosa have been affected, but for many years obstinate swelling and erosion of the lower lip has caused him the most distress. Heavy metals, antibiotics, vitamin E, and cortisone have been of little or no help to him, and he is sensitive to gold.

In August, 1952, he was given quinacrine hydrochloride (Atabrine dihydrochloride), 0.3 gm. daily, and after three weeks there was marked improvement. He took 0.2 gm. daily for another

two weeks and then stopped when the skin was stained yellow and the lip healed. This is the first time in eight years that the lupus of his lower lip has been quiescent.

On general examination there has been no evidence of systemic disease apart from the sedimentation rate at times being high (20 to 40 mm. in one hour). Blood cell counts, serological tests, and urinalysis have shown normal results.

In 1950, biopsy report revealed histological changes compatible with the diagnosis of lupus erythematosis.

DISCUSSION OF CASES OF DR. WELLS

DR. JOHN C. BELISARIO, Sydney, Australia (by invitation): I am delighted to be at this meeting and to meet so many old friends. I thank you very much for inviting me and for the very nice welcome you have given me.

We have been using quinacrine for some time in the treatment of chronic discoid lupus erythematosus, with a rather large proportion of success. In Britain in a series of over 100 cases investigators felt that in about one-third of the patients the lesions cleared entirely, one-third of the patients improved, and one-third were not influenced. They think that there is a place for quinacrine in the treatment. In Australia we have used it in a few cases. I think that the treatment is well worth while in spite of the quinacrine dermatitis that occasionally develops. In Britain I heard of two patients out of 100 in whom quinacrine dermatitis developed.

DR. LEON GOLDMAN, Cincinnati: I should like to discuss a small, rather unimportant facet, the use of 17-hydroxycorticosterone (Compound F).

In all our clinical experiments with local injection of 17-hydroxycorticosterone in facial lesions of lupus erythematosus, we have never used more than 2 to 5 mg., and not 25 or 75 mg., the dose which the first patient presented had. We have used only a small amount, and that could cause the fairly persistent but not permanent changes in the local area where 17-hydroxycorticosterone was injected. Only in tumor cases such as leukemia cutis and mycosis fungoides have we used the high concentration (25 mg.) and then with the Hypospray jet injection apparatus. Unfortunately, the supplies are limited. The oral free alcohol of 17-hydroxycorticosterone is better (more active dose for dose) in lupus erythematosus than cortisone, even in the discoid phase. I should like to ask what the lupus erythematosus spots look like under the Wood light after the use of quinacrine. Also I should like to know if the atrophic area which resulted from the 17-hydroxycorticosterone dose showed any fluorescence.

In reference to Dr. Wells's second case with the excellent response to quinacrine, a lupus erythematosus lesion on a lip is difficult to control. Some of this may be due to the protuberance of the lower lip with the development of an "exposure cheilitis." That is the reason why lupus erythematosus can persist on the lip and can even appear as the first mucocutaneous sign of systemic lupus erythematosus.

DR. THEODORE CORNBLEET: We, too, found that atrophy occurs after the local injection of 17-hydroxycorticosterone. The line of needle entry shows a persistent chamois colored raised narrow zone. The result is a stippling effect with multiple punctures and is not apt to enhance the appearance of the skin.

DR. GEORGE C. WELLS (by invitaton): Dr. Belisario has been able to draw upon a much larger experience of this treatment of lupus erythematosis, and I very much appreciate his observations. Of 12 patients with chronic discoid lupus erythematosis whom we have treated and observed over the last six months, nine were markedly benefited. The ones in whom the lesions cleared completely had had lesions for only a few months, and the resistant cases were those of many years' duration. We have treated one patient with disseminate lupus erythematosis with minimal signs of systemic involvement, and the lesions cleared up dramatically after four weeks of treatment. The response to quinacrine treatment is usually to be seen after about four weeks of treatment, by which time the skin is begining to be stained yellow. We do not yet know how long these remissions are going to last, but the response seems to be quicker than that which we see with gold treatment, and probably the toxicity will prove to be less than that of gold. Of course, we shall have to watch for toxic signs, such as skin eruptions of various types and blood dyscrasias.

Quinacrine treatment for lupus erythematosis was described by Page (*Lancet* **2**:755, 1951), and he reported good results in 14 out of 18 cases.

Concerning the fluorescence, the quinacrine begins to accumulate in the skin after about a week of treatment, and fluorescence under Wood's light is marked over the palms and nail beds. However, the discoid lesions also fluoresce brightly during the early weeks of treatment, and there may be some selective uptake of quinacrine in the skin lesions.

Injections with 17-hydroxycorticosterone (Compound F) were abandoned in the first case because of this apparently atrophy-producing effect. I am interested to hear from Dr. Goldman that we were injecting far too much, and I agree that further trials with small injections should be made.

Dr. Henry E. Michelson, Minneapolis: The quinacrine treatment of chronic lupus erythematosus is rather new. It was introduced to us recently by Dr. O'Leary at the meeting of the Minnesota Dermatological Society. Since then I have treated 27 patients with chronic discoid lupus erythematosus with this drug. The results I obtained are far from startling. Three of the patients had marked improvement. Several others noted that the lesions were paler but did not disappear. The best result was obtained in a patient with a hypertrophic destructive type of lesion. I also noted that in three patients with scalp lesions good results were obtained.

This drug should not be used for a patient who is acutely ill with systemic lupus. In fact, I do not think it should be used at all for a patient who has any constitutional symptoms. There seems to be no particular reason for its use. I judge that since quinine was used for lupus erythematosus someone decided to try this drug. Quinacrine has been used in Europe for the treatment of pemphigus, with no outstanding results.

For the moment I am not particularly enthusiastic about this treatment. I think that it should be evaluated in a conservative way.

Dr. Julius E. Ginsberg: For those who choose to use quinacrine hydrochloride (Atabrine Dihydrochloride) in the treatment of lupus erythematodes it would be of special interest to observe under Wood's light the characteristic yellow fluorescence of the nail beds of patients who are being given this medication. The fluorescence will not disappear for many months after the drug is withdrawn. (Ginsberg, J. E.: Wood's Light Fluorescence Phenomenon in Quinacrine Medication, *J. A. M. A.* **131:** 808-809 [July 6] 1946.)

Cutaneous Blastomycosis Treated with 4,4'-Stilbenedicarboxyamidine (Stilbamidine).

Presented by (by invitation) Dr. Lydia C. Marshak, Aurora, Ill.

W. C. H., a white man, aged 64, a machinist, has had large bright-red elevated lesions on his face for the past 2½ years. They have been asymptomatic and have not affected his general health. Local treatment has been ineffective. One year ago a biopsy was performed, and the diagnosis of blastomycosis made at the Copley Memorial Hospital in Aurora. He was given potassium iodide orally, the treatment resulting in gradual healing of the central parts of the lesions.

When first seen by me at that stage in June, 1952, the patient presented large flat serpiginous lesions on his forehead, cheeks, and chin. There was a wide bright-red heaped-up sloping border covered with minute crusted yellow verrucosities. The central areas showed scar formation. There was an ectropion of the right lower lid.

On Aug. 6, the patient was hospitalized and Stilbamidine Isethionate (4,4'-stilbenedicarboxamidine di-(β-hydroxyethanesulfonate) solution in isotonic sodium chloride was given by slow intravenous drip, starting with 0.05 gm., for two days, this dose being followed by a dose of 0.1 gm. of the drug for the next seven days. There was no immediate change in the lesions, but three weeks later a continuous regression of the active border could be observed. A second course of Stilbamidine was given intravenously from Sept. 13 through Sept. 22, and 0.1 gm. was administered for seven days, followed by 0.15 gm. for three days. The total amount of the drug given during both courses was 2 gm. There were no general complaints during or after treatment with stilbamidine.

Urine, complete blood cell count and blood chemistry (nonprotein nitrogen, urea clearance, and cephalin flocculation) were found to be within normal limits before, during, and after the treatment with Stilbamidine. The chest x-ray showed a normal picture.

Scrapings from the edge of the lesions were cultured on Sabouraud-dextrose agar at room temperature in June; a white aerial growth developed, which later became yellow-brown.

Cultures were retaken twice, after the second course of treatment, and so far, have not shown any growth.

A biopsy specimen is presented through the courtesy of Dr. P. Dolan, Copley Memorial Hospital. It was taken in Aug. 1951, and showed a pseudoepitheliomatous hyperplasia with intraepidermal abscesses and a dense polymorphous infiltrate in the corium, consisting of round cells, plasma cells, epithelioid cells, polymorphonuclear leucocytes, and a large number of giant cells; an occasional Blastomyces cell can be found in the cytoplasm of the giant cells.

Stilbamidine (4, 4′-Stilbenedicarboxyamidine) Therapy in Blastomycosis. Presented by (by invitation) DR. JACK RODRIQUEZ.

A. F., a white man aged 62, was presented before the Chicago Dermatological Society on May 12, 1952, and is being presented again to show the effects of Stilbamidine (4,4′-stilbenedicarboxyamidine) therapy.

Since 1942, when the diagnosis was first established, the patient has had extensive treatment with iodides and has received six x-ray treatments.

Before treatment with Stilbamidine was initiated, the diagnosis was reconfirmed by smears, cultures, and histologic sections which all revealed the presence of Blastomyces dermatitides.

In June, 1952, the patient was given one course of Stilbamidine by slow intravenous drip consisting of 50 mg. daily for two days, 100 mg. on each of the following two days, and 150 mg. daily for eight days. On completion of this first course of therapy, subjective improvement was claimed by the patient. Ojectively, the lesion was only slightly drier and flatter.

Two weeks later the patient was given a second course of Stilbamidine consisting of 150 mg. daily for 10 days. At the end of this course the patient's lesion showed unquestionable signs of involution. Healing has progressed slowly but continuously to the present time.

The Stilbamidine in all instances was administered in 500 cc. of 5% dextrose solution by the intravenous drip technique timed to be delivered in two hours.

Two weeks ago (and for the first time) the patient complained of numbness around his lips and mouth which is "just noticeable" but occasionally is annoying.

Before, during, and after Stilbamadine therapy urine, blood, nonprotein nitrogen, serum bilirubin, and cephalin and thymol flocculation tests have always been within normal limits.

There is hyperkeratosis and some flattening of the epithelium. In the corium there are loose perivascular infiltrates of lymphocytes and plasma cells and some vasodilatation. At one end of the section is a small papule with a somewhat denser infiltrate in the subpapillary corium.

There are residual chronic inflammatory changes, but there is now no evidence of blastomycotic granuloma.

DISCUSSION

DR. F. T. BECKER, Duluth, Minn.: Most of what I have to say I have learned from discussing this method of treatment with the instigator of this therapy, namely, Dr. A. C. Curtis of Ann Arbor (Curtis, A. C., and Harrell, E. R., Jr.: The Use of Two Stilbene Derivatives [Diethylstilbestrol and Stilbamidine] in the Treatment of Blastomycosis, A. M. A. ARCH. DERMAT. & SYPH. **6**:676, 1952). I have also treated several patients with this method of therapy and have also been gratified with the results. Dr. Curtis first became aware of the value of stilbene derivatives in the management of blastomycosis when two patients with carcinoma of the prostate gland were treated with diethylstilbestrol and showed a very favorable response as far as their blastomycosis infection was concerned. In looking for other drugs of a similar nature, he found Stilbamidine had a very marked fungicidal effect in the test tube. It is a rather toxic drug, but apparently it can be given safely in small doses, intravenously by drip. There have been several reports of involvement of the fifth nerve. Like streptomycin, it seems to have a predilection for the fifth nerve instead of the eighth. It is thought, however, that in cases localized to the skin without systemic involvement a trial administration with diethylstilbestrol should be made, rather than using the more toxic Stilbamidine, which should be reserved for the systemic cases.

DR. GEORGE C. WELLS (by invitation): I think that most of the toxic results have been on the fifth nerve and not the seventh and eighth. While some of these trigeminal neuropathies are serious, many of them are rather minor. The most serious aspect is the possible liver damage.

DR. LYDIA C. MARSHAK, Aurora, Ill. (by invitation): Stilbamidine has been given to thousands of patients with multiple myeloma and kala-azar in Africa and Asia. Most of them were poor risks. The high percentage of deaths may have been due to deterioration of the Stilbamidine during the transport from England. It is also well known that Stilbamidine becomes more toxic when exposed to light. The solution should be prepared immediately before the injection. Schoenbach and his associates, who introduced the use of Stilbamidine in blastomycosis, recommended the total dose of 4 to 6 gm., healing being not complete with a lower dose. In three out of his four patients trigeminal neuropathia developed. In the case presented today, the total dose given was 2 gm. The lesions have responded very well, and there have been no complications noticed so far.

DR. JACK RODRIQUEZ (by invitation): The toxicity of this drug is unquestionable, but is dependent upon the method of administration. If the drug is given by multiple syringe technique there is very little doubt but that the toxicity is very great, perhaps even dangerous. It is hepatotoxic and nephrotoxic, and it has an effect on the trigeminal nerve. In a large number of these patients who were treated neuropathy developed which consisted of numbness and/or creeping sensations on the skin. I think the important thing is that Stilbamidine should be administered by intravenous drip technique, given over a period of at least two hours and given in low concentration. We give 50 mg. for the first 2 days, 100 mg. the next 2 days, and 150 mg. through the 10th day. The drug is dissolved in 500 cc. of 5% dextrose in distilled water and timed to be delivered over a period of two hours.

Originally, the treatment was given by the multiple syringe technique. This modality produced sudden onset of circulatory collapse and later nephrotoxic and/or hepatotoxic complications and still later (three months) trigeminal nerve neuropathy. It is interesting to note that trigeminal nerve neuropathy complication occurs even with the low concentration intravenous drip techniques.

DR. RODRIQUEZ: Stilbamidine has been effective in nocardiosis and actinomycosis.

Congenital Ichthyosiform Erythroderma. Presented by DR. HAROLD SHELLOW.

DISCUSSION

DR. UDO J. WILE, Ann Arbor, Mich.: I think that this is an excellent example of this rather rare disease. This boy illustrates very well the stunting of growth and the musculature and bony structure as a result of this very unfortunate condition. No other siblings in the family have the same condition. Apparently, then, this is an isolated case in an otherwise normal child group.

Children with this disease look as though they had some serious form of deficiency. Their condition can be confused with some of the other exfoliative conditions found at birth, but failure to respond to treatment and the rapidity with which they succumb to exposure, usually to pneumonia or secondary infection, establishes the diagnosis.

DR. A. L. WELSH, Cincinnati: I should like to point out two possible complications in this disease. One comes from contamination with the herpes simplex virus and the other from cow-pox virus. In the former instance Kaposi's varicelliform eruption results, and in the latter vaccinia results. A Cincinnati family has seven members who have this type of eruption. Vaccinia developed in three of them after vaccination for variola during the bullous phase of the disease. The other members of the family were vaccinated during a nonbullous phase and vaccinia did not develop. In one of the members of the family Kaposi's varicelliform eruption developed after he had kissed a person with a lesion of herpes simplex.

DR. HERBERT RATTNER: In a newspaper some weeks ago there was a report from London of cure of this condition by hypnosis. Does anyone know more of this?

DR. GEORGE C. WELLS (by invitation): I come forward very reluctantly because this report has already received some newspaper notoriety, but I did see this case at a meeting of the Royal Society of Medicine about two years ago (Mason, A. A.: *Brit. M. J.*, **2**: 422, 1952). This 15-year-old boy had had severe congenital ichthyosiform erythroderma since birth, but of late there had been such acute hyperkeratosis of the palms and soles as to make his hands and feet almost useless, and treatment with salicylic acid ointments had been of little benefit. The

skin of the palms had been replaced by grafts from the trunk, where there were some normal areas, but the grafted skin had become as hyperkeratotic as that which it had replaced. It was suggested to the boy under hypnosis that the skin of the right arm would clear. This did happen about a week after the suggestion was made, and when I saw him the right arm was almost clear in sharp contrast to the other limbs. Further suggestion therapy under hypnosis has been given since, and although the skin is not entirely free of keratosis, remarkable improvement has been maintained over the past year.

I can offer no rational explanation of this, but can only say that it happened.

DR. STEPHEN ROTHMAN: None of the published hypnotic and suggestive experiments of this sort are well controlled. Who knows whether this patient did not apply some salicylic acid ointment to the "hypnotized" side?

DR. WELLS: Treatment with salicylic acid had been given before the hypnosis, but I understand that it was not being given during the suggestion therapy.

Chronic Porphyria. Presented by DR. OTTO C. STEGMAIER, Davenport, Iowa.

DISCUSSION

DR. STEPHEN ROTHMAN: I want to mention that Dr. Dillaha in our department had rather encouraging results with vitamin B_{12} in one case. The uroporphyrin excretion decreased, the hypertrichosis disappeared, the skin paled, the blister formation on the hands subsided, and the patient felt much better. It is true that the vitamin B_{12} administration coincided with the withdrawal of alcohol, but even after the patient resumed drinking her condition did not become worse as long as she took the vitamin.

DR. ROBERT KIERLAND, Rochester, Minn.: This is a good example of the condition that Dr. Brunsting and others have reported on numerous occasions, and in which decreased liver function is an almost constant finding. Our suggestion has been similar to that of Dr. Rothman's as far as treatment is concerned.

DR. MALCOLM SPENCER, Danville, Ill.: The relation between acquired photosensitivity and the bacterial flora of the stool has always been an intriguing problem. The late Dr. Eric Urbach stressed the importance of an abnormal stool flora in such cases. Urbach felt that in many of his cases hemolytic Streptococcus was present in the stool cultures and that by feeding viable colon bacilli he could restore the normal bacterial flora of the stool and thus help these patients with photosensitivity.

This may be of importance in this particular case, for the patient has noted diarrhea coexisting with exacerbations of her cutaneous eruption.

Recently in "Queries and Minor Notes" of *The Journal of the American Medical Association* (**150**:627, 1952) Dr. Albert Miltzer of Michael Reese Hospital suggested that if patients taking aureomycin or oxytetracycline (Terramycin) are given two teaspoonfuls of an elixir of vitamin B_{12}, folic acid and ferric ammonium citrate four times a day, neither the diarrhea nor the perianal irritation will occur. In addition, the consultant (Dr. Miltzer) suggested the use of suppositories consisting of 1½ grains (0.09 gm.) of sodium alkyl sulfate in theobroma oil (cocoa butter) as a suppository emulsion, which the patients inserts into the rectum three times a day.

I have recently had some experience with the use of a much simpler management of these diarrheas which occur after aureomycin and oxytetracycline therapy and with the management of the pruritus ani so often associated with secondary monilial infestations, by using a preparation containing Lactobacillus bulgaricus. We have had very prompt results with the ingestion of a tablet in a small portion of skimmed milk. Even with the concomitant taking of aureomycin or oxytetracycline these patients have noted a discontinuance of the diarrhea. My number of cases is small, but the response to the management has been quite remarkable. Within a period of 24 hours the normal stool is restored. One tablet is given three times a day with one-half glass of skimmed milk (Bu-Tabs, Hynson, Westcott & Dunning, Inc.).

DR. A. L. WELSH, Cincinnati: Are the bone marrow findings of any prognostic significance in cases of this type?

DR. UDO J. WILE, Ann Arbor, Mich.: Are there asymptomatic cases of porphyria?

DR. R. KIERLAND: There are definite cases of latent porphyria in that porphyrins may be demonstrated, but that the patient does not have clinical signs or symptoms. The families of

a number of patients of Dr. Brunsting have been checked and have been found to have latent porphyria.

DR. OTTO C. STEGMAIER, Davenport, Iowa: This patient originally presented blisters on the dorsum of the hand, together with hypertrichosis. The chief complaint today is frequent convulsions which occur every six to eight weeks. She also has pain in the chest, shortness of breath, and vague abdominal complaints, necessitating hospitalization 16 or 18 times in the last three years. In going back over the records she has had red urine on several occasions, but the presence of porphyrins was not suspected. Her mother, age 81, has no symptoms but does have red urine.

Watson and his co-workers have removed the spleen in some porphyrias associated with microcytic anemia, with good results. When this is applied to other cases without anemia, the results are not good. Experimentally, in England, Greyburger and Neu have treated patients with aminoacetic acid (Glycine) tagged with radioactive nitrogen. Their experiments demonstrated that porphyria is not due to the destruction of hemoglobin, but, rather, that is is an abnormality in the synthesis of hemoglobin.

Pemphigus? Presented by DR. HERBERT RATTNER, DR. HAROLD H. RODIN, and (by invitation) DR. STEFAN BIELINSKI.

DISCUSSION

DR. JOHN C. BELISARIO, Sydney, Australia (by invitation): I was especially interested in the woman with the extensive bullous lesions. Clinically, the case looks like pemphigus, while histologically it appears more like dermatitis herpetiformis. Recently, Percival, of Edinburgh, has done some more work involving 100 patients and has come to the conclusion that in 50% of the persons above the age of 55 who have dermatitis herpetiformis the disease has a fatal termination. He feels that a number of patients who die with a diagnosis of pemphigus may be shown to have had dermatitis herpetiformis, from a histological point of view, if enough sections are examined.

DR. M. R. CARO: Dr. Ebert and I have studied a number of these cases histologically and we have not found any consistent correlation between the histopathologic findings and the clinical course. Some of the cases showed very rounded tension bullae and yet eventually went on to terminate fatally as pemphigus. We have found acantholytic cells in cases that did not eventuate as pemphigus. I am not sure that pemphigus is a diagnosis that can always be made definitively under the microscope.

As to the statement that 50% of the patients with dermatitis herpetiformis die under a later diagnosis of pemphigus, I think that we must base our diagnosis of these cases on the clinical course, rather than on histopathologic findings.

Nevus Unius Lateralis? Lichen Striatus of 10 Years' Duration? Presented by DR. LOUIS RUBIN, Rockford, Ill.

Nevus Unius Lateralis. Presented by DR. MICHAEL H. EBERT and (by invitation) DR. ALLEN S. PEARL JR.

Nevus Unius Lateralis. Presented by DR. LOUIS RUBIN, Rockford, Ill.

Ectodermal Defect? Presented by DR. S. J. ZAKON and (by invitation) DR. B. J. PASS.

Pseudopelade? Persistent Alopecia Areata? Presented (by invitation) by DR. JACK RODRIQUEZ.

Erythema Gyratum Perstans (Colcott Fox); Erythema Figuratum Perstans (Wende); Amebiasis. Presented by DR. M. H. EBERT and (by invitation) DR. S. BARSKY.

Alopecia Areata of Peculiar Distribution. Presented by DR. EDWARD A. OLIVER and STAFF at Hines Hospital.

Erythema Multiforme; Possible Acute Lupus Erythematosus in Remission. Presented by DR. DAVID OMENS and (by invitation) DR. HAROLD OMENS and DR. J. F. SICKLEY.

Pemphigus Treated with Corticotropin (ACTH). Presented by DR. DAVID OMENS and (by invitation) by DR. HAROLD OMENS and DR. J. F. SICKLEY.

Dermatitis Herpetiformis. Presented by DR. DAVID OMENS and (by invitation) by DR. HAROLD OMENS and DR. J. F. SICKLEY.

Localized Calcinosis. Presented by DR. HERBERT RATTNER, DR. HAROLD RODIN, and (by invitation) by DR. STEFAN BIELINSKI.

Papulonecrotic Tuberculid? Presented by DR. DAVID OMENS and (by invitation) by DR. HAROLD OMENS and DR. J. F. SICKLEY.

Dermatomyositis. Presented by DR. JAMES R. WEBSTER, DR. SAMUEL BLUEFARB, and (by invitation) by DR. J. F. SICKLEY.

Discoid Lupus Erythematosus. Presented by DR. DAVID OMENS and (by invitation) by DR. HAROLD OMENS and DR. J. F. SICKLEY.

Case for Diagnosis (Hemosiderosis?). Presented by DR. M. H. EBERT and (by invitation) by DR. ALLEN PEARL and DR. STEFAN BIELINSKI.

Trophic Ulcer. Presented by DR. HERBERT RATTNER, DR. HAROLD RODIN, and (by invitation) by DR. STEFAN BIELINSKI.

CLEVELAND DERMATOLOGICAL SOCIETY

Irving L. Schonberg, M.D., *President*

John R. Haserick, M.D., *Secretary*

George M. Stroud, M.D., *Reporter*

Sept. 25, 1952

Sporotrichosis de Beurmann (Now Healed). Presented by DR. H. N. COLE; DR. J. R. DRIVER, and DR. H. N. COLE JR.

T. M., a 9-year-old boy, had an eruption on the right side of the neck and face of two weeks' duration. His home is in Green Springs, Ohio, next to a very large dense growth of timber, where there is a great deal of moisture and shade.

About May 1, 1952, an eruption, a little sore which became larger, developed, for which he was taken to his family physician, who gave him an ointment to use. The eruption began to get worse; it became swollen and began to ooze on the neck and on the side of the face. He was then given a boric acid wash and penicillin injections, under which treatment the eruption improved somewhat.

Later, at the time of the examination, there was a 1- by 2-cm. crust, surrounded by a subacute erythematous eruption, spreading behind the ear, on the right side of the face, and on the side of the neck.

Culture was taken on Sabouraud's medium to investigate the possibility of an actinomycosis or a sporotrichosis. He received several x-ray treatments, and seven days after the culture was taken the typical waxy wrinkled buff tan color, sometimes spoken of as "rattlesnake hide," appeared, and the patient was given potassium iodide internally, along with the x-ray treatments locally. With this process the eruption began to improve at once, and by July 29 it was nearly gone. No biopsy was taken.

The diagnosis of infection with the Sporotrichum schenckii was made.

DISCUSSION

DR. H. N. COLE JR.: When this boy was first brought into our office he had a lesion on the right side of the neck which appeared to be simply a furuncle. However, when it did not respond to symptomatic treatment or to antibiotic therapy we became suspicious and took a culture on Sabouraud's medium and got a culture of S. schenckii. When we asked about the history we found out that he came from a town in the western part of the state where there are many old trees, and his parents told us that he was in the habit of playing around them. Just before the meeting Dr. Haynes told me that he had read an article recently about an epidemic of 3,000 or 4,000 cases in persons working in a mine where they had wooden rafters and planks supporting the mine, and in these patients the source of the infection was traced and it was felt that perhaps it came from this rotted wood.

Chronic Porphyria with Cutaneous Manifestations. Presented by DR. S. I. SATO and DR. J. L. SECREST for the DEPARTMENT OF DERMATOLOGY, WESTERN RESERVE UNIVERSITY.

Adiponecrosis Neonatorum. Presented by DR. S. I. SATO and DR. J. L. SECREST for the DEPARTMENT of PEDIATRICS, UNIVERSITY HOSPITALS of CLEVELAND.

Tuberculosis Verrucosa Cutis? Presented by DR. G. W. BINKLEY and DR. F. M. MCDONALD.

Urticaria Pigmentosa (Unusual Type Acquired in Adulthood). Presented by DR. H. N. COLE; DR. J. R. DRIVER, and DR. H. N. COLE JR.

Fox-Fordyce Disease. Presented by DR. S. I. SATO and DR. J. L. SECREST for the DEPARTMENT of DERMATOLOGY, WESTERN RESERVE UNIVERSITY.

Pityriasis Lichenoides et Varioliformis Acuta. Presented by DR. H. N. COLE; DR. J. R. DRIVER, and DR. H. N. COLE JR.

Parapsoriasis en Plaque. Presented by DR. S. I. SATO and DR. J. L. SECREST for the DEPARTMENT of DERMATOLOGY, WESTERN RESERVE UNIVERSITY.

Lupus Erythematosus, Disseminata, Subacute. Presented by DR. S. I. SATO and J. L. SECREST for the DEPARTMENT of WESTERN RESERVE UNIVERSITY.

Mycosis Fungoides. Presented by DR. S. I. SATO and DR. J. L. SECREST for the DEPARTMENT of DERMATOLOGY, WESTERN RESERVE UNIVERSITY.

Pemphigus Erythematosus. Presented by DR. S. I. SATO and DR. J. L. SECREST for DR. G. M. STROUD.

Follicular Lymphoma or Lymphocytoma Cutis. Presented by DR. ALLEN E. WALKER and DR. JOHN J. STEWART.

Congenital Defect of the Scalp. Presented by DR. ALLEN E. WALKER and DR. JOHN J. STEWART.

Congenital Circumscribed Skin Defects (Congenital Aplasia or Atrophia Cutis Circumscripta). Presented by DR. H. N. COLE; DR. J. R. DRIVER, and DR. H. N. COLE JR.

Dermatomyositis. Presented by DR. H. N. COLE; DR. J. R. DRIVER, and DR. H. N. COLE JR.

Chronic Porphyria with Cutaneous Manifestations. Presented by DR. S. I. SATO and DR. J. E. SECREST for the DEPARTMENT OF DERMATOLOGY, WESTERN RESERVE UNIVERSITY.

Irving L. Schonberg, M.D., *President*

John R. Haserick, M.D., *Secretary*

George M. Stroud, M.D., *Reporter*

Oct. 23, 1952

Lichen Myxedematosis. Presented by DR. JOHN BEMBENISTA and DR. JULIUS KANZEL (for DR. J. E. RAUSCHKOLB).

W. D., a 42-year-old white man, was presented in 1950 with a history of development of nodules on the elbows beginning in 1948. There was progression of the lesions to the extensor surfaces of the wrists, knees, abdomen, and the cervical region. Since 1950, these lesions have become generalized. The patient had bilateral congenital cataract extractions in 1935.

The eyes show a pendular nystagmus and a bilateral absence of the lens. On the skin there is a generalized distribution of pinhead to split-pea-sized firm nontender mostly discrete papules and nodules. There is a tendency toward grouping and coalescence over the extensor surfaces of the elbows, knees, and other bony prominences.

X-ray examination of the heart, sella turcica, and skull showed normal findings. Hemogram, urinalysis, Kline serologic test for syphilis, basal metabolic rate, blood cholesterol test, sodium, potassium, and total protein determinations all showed results which were within normal limits.

Histologic examination of the skin showed in the upper corium three well-defined foci, composed of interlacing bundles of fibroblasts and collagen, among a loose, fibrillar, and granular basophilic matrix. A few stellate cells were present. The epidermis overlying the foci showed flattening of the rete pegs. Section stains revealed a moderate amount of mucin in the foci and an absence of fat and amyloid.

No treatment has been given.

DISCUSSION

DR. B. P. PERSKY: In 1950 there was some question about accepting the histologic evidence of myxedema. I think that he was presented with the diagnosis of papular myxedema. Since that time the disease has extended and I think it looks more typical than it did. He still has not had any itching. The slides today showed a definite positive result for mucin, with the carmine stain. I think that the diagnosis is myxedema, and more adequate terminology would be lichen myxedematosis without any internal complications of serious nature, as far as we can tell. The findings of the endocrinology department did not fit into a pattern from which they could make a diagnosis.

DR. G. A. DE OREO: This man exhibits the myxedematous changes of typical early cases, and in those cases one usually finds hypofunction of the thyroid. His basal metabolic rate seems to be normal. I wonder if he should be given some thyroid medication.

DR. H. N. COLE: Another thing which would help to substantiate the diagnosis would be to give an injection of hyaluronidase.

DR. P. CHIVINGTON: Two years ago we did inject hyaluronidase in the lesions, and we were unable to tell whether or not there was any change following that procedure. I think that the point of resolution of the lesions is somewhat controversial. I believe that it has been claimed also that they do not resolve. Rather extensive amyloid studies were done at that time, and all the tests showed negative results.

DR. I. L. SCHONBERG: Could a test with radioiodine to determine thyroid deficiency be done? The lesions on the upper extremities are like those described by Wise and Rein, which they called lichen ruber moniliformis. The generalized reaction in this case is suggestive of that.

DR. H. A. HAYNES: It is my understanding that these cases of even localized myxedema usually occur after the thyroidectomy in a patient with hyperthyroidism, and it is usually due to the sudden removal of the thyroid tissue and the unopposed action of the pituitary thyreotropic hormone. One would think, then, that it would help if one could neutralize the effect of the thyreotropic hormone. It has been suggested that thyroid helps very little in the treatment of myxedema, but that occasionally thyroxin or even estrogen might help.

Epidermal Dysplasia Verruciformis of Lewandowsky and Lutz. Presented by DR. BENJAMIN P. PERSKY.

Generalized Scleroderma. Presented by DR. JOHN BEMBENISTA and DR. JULIUS KANZEL (for DR. J. E. RAUSCHKOLB).

Tuberculosis Cutis Colliquativa Occurring After Tuberculous Osteomyelitis. Presented by DR. JOHN BEMBENISTA and JULIUS KANZEL (for DR. J. E. RAUSCHKOLB).

Senile Keratosis with Bowen's Type Degeneration. Presented by DR. GEORGE H. CURTIS and DR. KENNETH H. BURDICK.

Dermatitis Repens. Presented by DR. JOHN BEMBENISTA and DR. JULIUS KANZEL (for DR. J. E. RAUSCHKOLB).

Superficial Basal Cell Carcinoma. Presented by DR. JOHN BEMBENISTA and DR. JULIUS KANZEL (for DR. J. E. RAUSCHKOLB).

Case for Diagnosis. Presented by DR. GEORGE H. CURTIS and DR. E. S. KOZIKOWSKI.

Lichen Scrofulosorum. Presented by DR. JOHN BEMBENISTA and DR. JULIUS KANZEL (for DR. JOHN E. RAUSCHKOLB).

Subacute Disseminated Lupus Erythematosus. Presented by DR. JOHN BEMBENISTA and DR. JULIUS KANZEL (for DR. J. E. RAUSCHKOLB).

Case for Diagnosis (Erythema Multiforme?). Presented by DR. JOHN BEMBENISTA and DR. JULIUS KANZEL (for DR. J. E. RAUSCHKOLB).

Tinea Capitis with Kerion Formation and Trichophytid Reaction. Presented by DR. JOHN E. RAUSCHKOLB.

Case for Diagnosis (Parapsoriasis en Plaque [Brocq]?). Presented by DR. JOHN BEMBENISTA and DR. JULIUS KANZEL (for DR. J. E. RAUSCHKOLB).

MINNESOTA DERMATOLOGICAL SOCIETY

Elmer T. Ceder, *President*

Harold G. Ravits, *Secretary*

Mayo Clinic Meeting, Sept. 14, 1952

Dermatomyositis.—R. Y. a woman, aged 41, had urticaria, edema, erythema, and Raynaud's phenomenon of the hands at the age of 32. At age 35 examination here showed generalized erythema and thick keratinization of soles. A biopsy confirmed the clinical impression of pityriasis rubra pilaris. The same diagnosis had been made elsewhere. An x-ray of the chest showed diffuse miliary infiltrations. Multiple guinea-pig inoculations gave negative results.

During the next year and a half atrophy of the shoulder muscles with generalized erythema and desquamation developed. Muscle biopsy revealed dermatomyositis. Skin biopsy revealed "atypical lichen planus." X-ray of the hands showed acrosclerosis, with calcinosis in the fingers. An esophageal x-ray showed a negative picture. Analysis of 24-hour urine specimens revealed preformed creatinine, 340 mg., and creatine, 167 mg.

Six months later (March, 1949) she exhibited marked skin changes of the poikiloderma type. At this time her preformed creatinine was 583 mg. and the creatinine was 457 mg. on 24-hour urine specimens. The sedimentation rate at this time was 68 mm. per hour, the highest noted during the course of her illness. Since she was seen in March, 1949, there has been a steady progression of the disease, with the development of calcific deposits about the shins, knees, fingers, and elbows.

Dermatomyositis (previously presented in 1936 [ARCH. DERMAT. & SYPH. **35**:986, 1937]).—This 25-year-old patient was first seen here 17 years ago (1935) with dermatitis simulating acute disseminated lupus erythematosus. One year later generalized muscular pains with painful stiff ankles, knees, and fingers, cachexia, puffy face developed, followed by marked muscular atrophy of the extremities. Skin biopsy revealed toxic dermatitis.

The dermatomyositis became quiescent in 1942 with the onset of Cushing's syndrome, for which a bilateral adrenalectomy was performed with satisfactory results. The pathological report was adrenal cortical hyperplasia.

Elsewhere, multiple operations such as capsulectomy and fasciotomy were successfully performed in 1943.

Recently there has been no marked clinical change.

DISCUSSION

DR. CURTIS, Ann Arbor, Michigan: These two cases were very striking. I have never before seen the combination of Cushing's syndrome and dermatomyositis. The resulting extensive resolution of the dermatomyositis and the subsequent atrophy of almost the entire skeleton allow one to speculate on the fact that when the Cushing syndrome in this woman developed her dermatomyositis disappeared. One wonders whether or not the steroids might not be given in larger amounts to these patients. Even though this patient had an operation on the adrenal cortices for her Cushing's syndrome, hirsutism and the physical characteristics of the disease are still present.

DR. PAUL O'LEARY, Rochester: These two cases were presented to precipitate a discussion on the various systemic manifestations of dermatomyositis, rather than the dermatologic features of the disease. The case of the first patient presented was diagnosed originally as pityriasis rubra pilaris by a number of dermatologists in Chicago, diagnosis of which was confirmed on her first admission here. As the pityriasis rubra pilaris faded, she then manifested signs of acrosclerosis, which in turn was followed by the development of a picture of dermatomyositis. In other words, she today has sclerodermatomyositis.

The second patient, who has been under our care for many years, had a pseudo Cushing's syndrome with virilism approximately 5 years after the onset of her dermatomyositis. She had an adrenalectomy in 1942, at which time one adrenal gland was completely removed and seven-eighths of the other one. She has had no steroid therapy.

Recently, case reports have been made of patients with visceral carcinoma occurring as a terminal manifestation of the dermatomyositis, and we have three cases in which a Cushing-like syndrome developed during the course of the disease. The Cushing's syndromes were not terminal in our cases, while the carcinomas were. Accordingly, in patients with dermatomyositis, visceral disease of one type or another should be anticipated.

The second patient has been invalided for many years and, as you saw, most of her muscles are now ribbons or remnants, and the joint fixations have been materially helped by orthopedic surgery. When we presented this patient before this society in 1936, I thought that dermatomyositis was an infectious disease, but observation of many patients since that time has not supported this idea. Today, our problem is to determine whether the carcinomas and the adrenal diseases are an incidental complication, a late sequelae, or an etiologic factor in the syndrome we call dermatomyositis.

Pemphigus Vulgaris Dermatitis Herpetiformis. Case for Diagnosis: Bullous Eruption.

DISCUSSION

DR. HENRY MICHELSON, Minneapolis: I would rather discuss these patients collectively than discuss any particular one. In all problems of dermatology we are stimulated by some event, and we then give a particular disease a lot of attention; for example, the discovery of the Hargraves cell made us concentrate on lupus erythematosus. Now, with the new interest in the pathology of pemphigus we have taken on a new momentum in studying that group. What comprises the group? We have to differentiate between those diseases which are preeminently bullous and those in which bullae occur occasionally. I heard Dr. Ockuly state that he thought his patient had a toxic bullous eruption. We hear such a statement made frequently, and still it is very hard to explain just what we mean by such a diagnosis. By and large, toxic eruptions are erythematous or urticarial and simulate drug eruptions. They are rarely bullous, although one must admit that such extreme examples do exist. The same is true for erythema multiforme. I have seen very few cases of frank erythema multiforme in which there were bullae. For my own part, I do not classify erythema multiforme as a bullous disease. I am amazed at the number of things clinicians classify under the heading of erythema multiforme. Dermatitis herpetiformis, if one uses strict criteria of morphology, does not show bullae very often. It is a polymorphous eruption and has striking subjective symptoms. I think that we have reached a stage when we are no longer able to diagnose frank bullous eruptions without a very careful microscopic analysis. The question then presents itself, are we willing to confine the diagnosis of pemphigus to those patients whose lesions show true acantholytic bullae or

cells? If so, what are we going to call the disease which has a bullous eruption, no subjective symptoms of dermatitis herpetiformis, and a pressure type of bullae microscopically? Must we wait to see if the patient survives? But if he does not, are we willing to state that there are cases of pemphigus in which there are no acantholytic bullae? I doubt if we are in a position to make a decision at this time. I hope that people like Dr. Brennan and Dr. Fisher will continue their studies, so that we may be able to come to some decision.

DR. H. MONTGOMERY, Rochester: The material presented on bullous dermatoses at the suggestion of Dr. O'Leary at this meeting simply represents at most a preliminary report. Our interest was stimulated by Arthur Rook's visit to us in April of this year; he had had the opportunity of working with Civatte. Civatte, in 1936, and later, in 1938 and 1943, distinguished various forms of pemphigus from other bullous dermatoses on the basis of acantholysis, and, more recently, Tzanck has described a cell in the blister fluid of pemphigus which when present is regarded as diagnostic and, according to many authors, differs from the balloon cells seen in herpes zoster, varicella, and possibly even in variola. Articles by Dupont and Pierard, together with various articles by Civatte, and articles in the United States recently in the A. M. A. ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY by Lever, Director, Winer, and Lipschultz, and a brief article by Rook and Whimster (*Brit. J. Dermat.* **62**:443-446, 1950) review the different concepts. (There are also many other articles in the French and Belgian literature.)

There can be no question but that the different forms of true pemphigus are characterized by acantholysis, including lysis of the individual cells, through various degenerative changes and intracellular edema and loss of prickles and intercellular bridges. Pemphigus vulgaris chronicus is used by Lever and is used on the continent, according to Rook, to designate what is essentially dermatitis herpetiformis and is a pressure or tension bulla without any of the phenomena of acantholysis. There are apparently two types of pemphigus vegetans; one type, which Hallapeau described, which probably in this country would be called dermatitis vegetans and which runs a benign course. Rook emphasized that it is not so important to consider whether bullae occur within the epidermis or subepidermally, and I have seen tension bullae of dermatitis herpetiformis occur within the epidermis, although they are usually subepidermal. Dupont, in an article in the *French Annals of Dermatology*, 1951, distinguishes benign pemphigus of Hailey and Hailey on the basis that the acantholysis shows no lysis or degeneration of the prickle cells that are lying freely in spaces, nor does benign pemphigus show the phenomenon of corps ronds or grains of Darier's disease. I would agree with their point of view that pemphigus erythematosus (Senear-Usher syndrome) histologically fits in with other forms of pemphigus and also reveals acantholysis, and that Darier's disease is not related to benign pemphigus. Dermatitis herpetiformis, bullous erythema multiforme (whether due to allergies to drugs or not) and bullous lupus erythematosus all present tension or pressure bullae. Various forms of true pemphigus, variola, varicella, and the herpes zoster group present acantholysis. Dr. Joe Brennan by artificial reproduction of blisters with cantharides on apparently normal skin obtained an acantholytic blister in three cases of pemphigus, but only tension bullae in cases of dermatitis herpetiformis and other dermatoses causing tension bullae.

The definition of acantholysis is wrong in "Diseases of the Skin," by Ormsby and Montgomery, as is the histologic illustration of pemphigus. When Dr. Rook was here, we spot-checked some fifteen cases, and he made a histologic diagnosis in each of them. Then we checked the histories and found that there had been erroneous diagnoses of pemphigus in many cases, because the bullae were clear and did not have any cells, but the bullae did not show acantholysis. The patients were alive and well many years later. In one such case, demonstrated at the Minnesota Dermatological Association in 1927, and in which there was a question raised at the time of dermatitis herpetiformis and erythema multiforme, the lesions cleared up in 2 years, and the patient was alive and well 13 years later.

It is not correct or right to draw too fine a distinction on the basis of one laboratory procedure, namely, histopathologic studies in a given case of bullous dermatosis. I think, however, that we have come to the point where if acantholysis is present and the virus diseases such as the varicella herpes zoster group are ruled out, we are warranted in making a diagnosis

of pemphigus rather than dermatitis herpetiformis or erythema multiforme. The failure to demonstrate acantholysis in a single biopsy specimen, would not, however, specifically rule out the diagnosis of pemphigus.

DR. I. FISHER, Minneapolis: We also are studying a number of patients with bullous eruptions. Our effort is to determine how consistently the acantholytic cell is found in patients who have a clinical diagnosis of pemphigus. Our effort also is to correlate the clinical picture with the finding of the acantholytic cell in order to know whether or not this microscopic finding occurs consistently in those cases that terminate fatally. The question arises as to whether or not there is the acute form of pemphigus with the acantholytic cell and the more prolonged form that does not demonstrate this cell. If one is to make the distinction beween pemphigus of the acute form and the more chronic form with tension bullae, one wonders whether it is proper to group these with dermatitis herpetiformis. This removal from the pemphigus group and transferring to the dermatitis herpetiformis group is simply the transferring from one basket to another, without any clarification of the problem. If, on the other hand, one considers that the more chronic form with the tension bullae represent a third disease, our feelings are pretty well covered in Dr. Michelson's discussion.

DR. SAMUEL J. ZAKON, Chicago: As I listened to Dr. Michelson's discussion, I was reminded of the original paper of Nikolsky (Nikolsky, P. V.: Data for the Study of Pemphigus Foliaceous, Univ. Izviestiya, Kiev. 1896) on pemphigus. In this paper, published in 1896, Nikolsky had five plates with sections showing acantholysis very much like the beautiful exhibit of Dr. Montgomery. Then he observed in all of his cases that upon tension of the epidermis he is able to remove the stratum corneum and granulosum from the skin of patients in whom he made a diagnosis of pemphigus. It shows how little we have advanced in our knowledge of the etiology of pemphigus that he in 1896 and we in 1952 are still struggling with the same problem.

Localized Myxedema.—M. T. V., a woman aged 27, had exophthalmic goiter of four years' duration and pretibial edema of one year's duration. She had been taking 2 grains (0.12 gm.) of thyroid daily for the past two years.

Skin biopsy of the right leg revealed myxedema.

Her basal metabolic rate was + 29 on March 11, 1952, and — 8 on May 16, 1952.

Subtotal thyroidectomy was performed in March, 1952. Concurrently, local injections of hyaluronidase were started, totaling 1,600 viscosity units in three weeks to the plaque on the left leg, resulting in some clinical improvement over the untreated right leg. Subsequently 1,000 viscosity units were given for both legs within the next two weeks.

DISCUSSION

DR. ARTHUR C. CURTIS, Ann Arbor, Mich.: These were striking cases. I have never seen so extensive a localized myxedema as in the second case exhibited. It resembled a severe lymphangitis in appearance. Both patients had had thyroidectomy, both had exophthalmos, and in both the localized myxedema developed before operation. However, each one had had a "medical" thyroidectomy, because both had been given propylthiouracil for some time before the operation. The patient with the most exophthalmos and the least solid edema had been given this drug for the longest period, having taken it for about a year before operation. The second patient had also taken the drug for a period of months. These patients also illustrate the fact that when one has a malignant exophthalmos one need not have the retraction of the upper lid so that the sclera is seen above the cornea. The palpebral fissure will appear on casual examination to be perfectly normal. When one examines the eyes from the side, a definite protrusion of the eyeball is seen. If the exophthalmos is measured by an exophthalmometer, a definite exophthalmos is found. In a survey done by Dr. Bierwaltes, of all the patients with progressive exophthalmos he has had under treatment 50% have also had localized myxedema. He is treating the patients who have progressive exophthalmos with desiccated thyroid, irradiation to the pituitary gland, and the female sex hormones. A fairly large percentage of patients with progressive exophthalmos and localized myxedema are women.

DR. F. T. BECKER, Duluth: I have always wondered about the localization of myxedema. It is nearly always on the anterior legs, and I have always thought that trauma was a factor. I studied the case of one patient at the University of Minnesota in 1935 who had unfortunately slipped and fallen on the ice and who later came under my care. He was unconscious for several hours in subzero weather, freezing both hands and feet. Localized myxedema later developed in these areas.

DR. PAUL A. O'LEARY, Rochester, Minn.: In the first group of these patients I saw many years ago, it seemed that the edema of the legs, which developed during the active phase of the hyperthyroidism, played a prominent role in the production of the localized myxedema or solid edema. They were patients who had severe hyperthyroidism, with exophthalmic goiter and with cardiac involvement, resulting in pronounced edema of the lower legs, most of whom had undergone surgical thyroidectomy. Dr. Henry Plummer objected to the use of the term localized myxedema at that time because he could not conceive of a localized myxedema developing in a patient with hyperthyroidism, so that it was three or four years before he would consent to my recording these cases in the literature. Since that time I have seen these edematous plaques without preceding edema develop in patients who have not had thyroid surgery and in whom the degree of hyperthyroidism was mild.

Dr. Curtis, as you recall, suggested recently the possible relationship between the thyroid and the pituitary in the development of these lesions.

Another point worthy of emphasis is that in most of the cases of localized myxedema that I have followed for a long time the lesions have eventually involuted spontaneously, some doing so seven or eight years after the onset. Therefore, I believe that caution must be used when we are evaluating any therapeutic program for this condition.

Dr. Curtis mentioned that hyaluronidase is not effective.

DR. H. MONTGOMERY, Rochester, Minn.: More mucin was present in the biopsy specimen taken after hyaluronidase had been given to one of the patients than in the biopsy specimen taken before treatment was instituted.

Generalized Moniliasis.—L. H., a girl aged $4\frac{2}{12}$ years, had a normal birth. Onset of extensive oral thrush occurred at $2\frac{3}{4}$ years of age. There was a rapid spread to face and scalp at $3\frac{2}{12}$ years of age; at the same time there was an onset of productive cough and bouts of high fever. This episode was treated as a pneumonia with multiple antibiotics, including aureomycin. Varicella occurred at $3\frac{5}{12}$ years of age, accompanied and followed by convulsions. Convulsions ceased when Asterol (2-dimethylamino-6-[beta-diethylaminoethoxy]-benzothiazole dihydrochloride) ointment therapy was discontinued. For the past nine months, the skin lesions have spread, but the patient has improved insofar as her general health is concerned.

The blood sugar was 78 mg. per 100 cc. on Oct. 13, 1952.

Chest x-rays on four occasions, and as recently as July, 1952, have shown infiltration in both bases, suggestive of bronchiectasis. (The child had pneumonia many times during the first year of life.)

Cultures for Candida albicans from sputum, skin scrapings, and stool gave repeatedly positive results. Culture of spinal fluid did not grow C. albicans. The spleen was enlarged.

DISCUSSION

DR. MAURICE REUTER, Milwaukee: In two or three cases of generalized cutaneous moniliasis in children that I have had the opportunity to observe, some difficulty was experienced in differentiating this disease from epidermolysis bullosa. Clinically there were usually marked oozing crusted lesions, especially on the face and extremities, suggesting an extensive pyoderma. In addition, the children had sparse scalp hair, and organisms could not be recovered from the scalp.

In one case which I saw fairly early and which I followed for a time, the child's lesions were finally cleared after several years by the use of diiodohydroxyquinoline (Diodoquin), which was prescribed by the general practitioner who had taken charge of the case. This drug is an iodine preparation, relatively nontoxic, and is apparently a parasiticide.

Since in the case shown there has been resistance to therapy, which is what usually occurs in this disease, I suggest that this drug be tried.

DR. ARTHUR C. CURTIS, Ann Arbor, Mich.: The stilbamidine group of drugs is also called the aromatic diamidines. Their formula consists of two benzene rings attached by central carbons and an NH group attached to each central carbon atom. When one looks at the chemical structure of those substances, they resemble diethylstilbestrol. The English have done most of the work with this group of compounds in bacterial and trypanosome infections. Their effect on bacteria is very similar to the effect of the sulfa drugs, and the chemical formula somewhat resembles that of the sulfa drugs. Diethylstilbestrol, which is not a true hormone but a stilbene with a hormone-like action, is so closely related chemically to stilbamidine that we used both compounds in the treatment of blastomycosis, with excellent results. Recently, several stilbenes, as well as many of the hormones and other compounds, such as isonicotinic acid, have been studied in vitro by our group in the superficial and deep mycoses. This study again upholds the work of Elson, who in a brief in vitro survey found stilbamidine effective in blastomycosis, but not in moniliasis. Neither diethylstilbestrol, isonicotinic acid, nor the male or female sex hormones have any effect on Candida in vitro. In a survey recently completed in our laboratory on the in vitro effect of diethylstilbestrol on a group of superficial fungi, this compound produced inhibition of many of the superficial fungi in amounts of 0.01 mg. per milliliter.

DR. STURE JOHNSON, Madison, Wis.: The skin changes, the presence of C. albicans, and the course of the disease, except for absence of persistent diarrhea, suggest acrodermatitis (Danbolt) enteropathica (*Acta. dermat. venereol.* **23**:127, 1943). In this condition diiodohydroxyquinoline has been found to be a better form of iodine therapy than potassium iodide.

DR. R. R. KIERLAND, Rochester, Minn.: We have not used diiodohydroxyquinoline. We have used iodine locally, without success. This child has been given diethylstilbesterol for three months, with no improvement. Endomycin, a new antibiotic which has some promise in the treatment of moniliasis, will be tried next.

DR. MARVIN S. KAGEN, Appleton, Wis.: Dr. Erich Seligman injected mice intraperitoneally with C. albicans. Some received aureomycin before the injection, and others received aureomycin after the injection. The mice that received the aureomycin before the injection died, while the mice that received aureomycin after the injection survived. Aureomycin stimulates the growth of C. albicans on culture media. These findings indicate a stimulation of the growth and action of C. albicans by aureomycin. With the wide use of antibiotics, we can expect to see more cases of systemic moniliasis.

Ragweed Dermatitis.—C. A. S., a farmer, aged 68 years, had chronic lichenified and excoriated dermatitis, sharply limited to the face, neck, and left arm. The first onset was in February, 1952, after he had been cleaning a silo, and the lesions had been persisting off and on, being aggravated particularly after contact with farm dusts. There were no other allergic manifestations. Patch tests gave a positive reaction to ragweed, small and Western, also to burweed, cocklebur, and sage. Scratch test gave a negative result to common dusts, including ragweed.

DISCUSSION

DR. J. B. HOWELL, Dallas, Texas: I should like to call attention to the fact that ragweed dermatitis can mimic very closely atopic dermatitis. This has been observed a number of times, most recently in a 9-year-old girl who presented an eczematous dermatitis of the feet and lower extremities. Her history and the morphea of the eczema suggested atopic dermatitis. Patch tests revealed that she was allergic to bitterweed, sneeze weed, and cocklebur.

The terminology in cases of weed dermatitis is a minor point, but it deserves mention. Throughout the literature the diagnosis "ragweed dermatitis" is applied to cases in which the patients have been found to be allergic to ragweed alone, to ragweed and one or more other weeds, and to weeds other than ragweed. Would it not be preferable to use "ragweed dermatitis" when ragweed alone is found to be the offending contactant and to speak of cocklebur, parthenium, bitterweed, marshelder, etc., dermatitis when the particular plant is found to be at fault?

DR. J. B. CEDER, Minneapolis: What do you think of sensitization therapy?

DR. J. B. HOWELL, Dallas, Texas: This patient is going to be in trouble if he does not move away from his farm. I do not think that he can avoid weeds sufficiently to remain free of the

dermatitis. The Shelmire method of oral desensitization, that is, increasing one's tolerance to plants by orally ingesting the specific oils, is effective in the majority of cases in which it is carried out properly. The patch-test reactions to the specific plants will not be reversed to negative when the oleoresins are taken orally. The oleoresin therapy should be started after the dermatitis has cleared completely. It should be emphasized that the procedure should be repeated each winter. When carried out properly over several years, the oral method of increasing one's tolerance to weeds will be more effective the second, third, and fourth years than the first year. Many farmers have been able to continue their work and have not had to change their environment by taking the specific oleoresins orally. Of course, every effort should be made on the part of this patient to avoid weeds, hay, feed-stuff, and indirect exposures, such as contacting cattle. A number of farmers who are sensitive to weeds are also sensitive to insecticides which contain pyrethrum, citronella, and/or DDT.

In defense of my statement that weed dermatitis is due almost entirely to contact with plant directly or indirectly and that the pollen plays no role in sensitizing the subject and a very minor role, if any at all, in accentuating or prolonging the dermatitis, may I state the following? The majority of weeds which have a high sensitizing capacity have negligible amounts of air-borne pollen. Patients with dermatitis from weeds having wind-borne pollen fare well and do not have exacerbations during the pollen season if they move to the city and successfully avoid direct or indirect contact with the offending plant or plants. Indirect contact with plant oleoresins from contaminated clothing, shoes, cattle, hair, and feedstuff is easy to overlook. Failure to realize that weed dermatitis is commonly a polyvalent sensitization and may include other contactants such as insecticides (pyrethrum) can lead to falsely blaming pollen rather than an insecticide for a given exacerbation.

Rarely does one know when one is exposed to poison ivy, for example. This is equally true with contacts made with other plants. In Texas we find as many people who are allergic to parthenium as to ragweed, yet parthenium produces a negligible amount of air-borne pollen. The clinical course of weed dermatitis is essentially identical in two patients—one in whom the dermatitis is caused by a plant which has a large amount of air-borne pollen (ragweed and marshelder), and another in whom the sensitization is caused by a plant which has a negligible amount of air-borne pollen, namely, parthenium and cocklebur.

Dr. George Brock, Winnipeg, Man., Canada: I was interested in Dr. Howell's remarks that ragweed dermatitis occurs preeminently from contact with the weed rather than from the air-borne pollen. In our flat prairie city, most of the city residents who have pollen dermatitis are bus drivers, streetcar motormen, truck drivers, and policemen. They are exposed to the air-borne pollen, but not to the weeds. On the other hand, railway right-of-way laborers have been seen with contact dermatitis on the hands and ankles from direct contact with the weeds. The ones sensitive to the air-borne pollen present a symmetrical diffuse eruption on the exposed parts and the flexures.

Dr. L. A. Brunsting, Rochester, Minn.: This man gives the characteristic history of ragweed dermatitis in that the disorder first appeared in adult life after overwhelming exposure to farm contacts, in this instance, the dust that was generated while he was cleaning the silo. Since this is his first experience with ragweed dermatitis, no seasonal incidence can be noted. He has no history or record of other allergic manifestations, and scratch tests with the protein fractions of common dusts and inhalants gave negative results. On the other hand, patch tests to small ragweed, cocklebur, burweed marshelder, and sage gave positive reactions. The patch reaction to giant ragweed is negative, as is usually the case. I am not too impressed by the benefits obtained in such patients following attempts at desensitization by means of the oral administration of the fat-soluble extracts of the particular plants to which the patients are sensitive. It is true that some persons feel better after such treatment, but there is no way to measure the effect, and the results may be ascribed to variations in the natural course of the disease or the fact that the patient avoids contacts which he now knows to be harmful to him. This man, like so many others, had received elsewhere a long series of injections of house-dust antigen. I have never seen this procedure bring about any benefit in dermatologic cases.

Erythema Induratum.—F. Z. is a 49-year-old farmer's wife with a 15-year history of recurrent painless nodules and scarring ulcers on the right lower leg. The ulcers have taken

a chronic course, healing in one to four years. In 1949, a biopsy was said to reveal tubercle bacilli, and streptomycin therapy was given for four months, without effect. In 1951, another biopsy was reported as showing no tubercle bacilli. At present, the patient has a sharply demarcated ulcer which began two years ago. Her general health has been unimpaired.

DISCUSSION

DR. HENRY MICHELSON, Minneapolis: As the field of dermatology grows and expands one of the dangers is conformity, and I think that it is very easy for all of us to follow a line and not resist diagnoses which are obvious but not certain. I was glad when Dr. O'Leary and Dr. Montgomery read a paper on vascular nodosities. I am sure that they are aware that the paper provoked a lot of comment and has been quoted very broadly. They knew, as many have before, that lesions that looked like erythema induratum but could not be proved to be tuberculous in origin should not be called erythema induratum, which term is confined to a condition which is due to tuberculosis. In the microscopic examination where lesions have their origin in the hypoderm, the term wucher atrophie has been used a great deal and has been popularized. I took the trouble to investigate how this term came into the literature and found it was done by Flemming of Berlin many years ago, but he did the work when he was investigating the loss of fat in emaciating disease. A Japanese student whose name, I believe, was Shadaki, worked in Jadassohn's laboratory and tried to apply Flemming's theory to the findings in the cases of erythema induratum. Wucher atrophie is certainly not an atrophy. It is a replacement of fat by an infiltrate and occurs in almost any type of infection involving the fat. I think that Dr. Montgomery will agree that it is very difficult and maybe impossible to diagnose erythema induratum by the microscope alone. Dr. Brunsting brought up the treatment of tuberculosis of the skin as he heard of it in Europe. I am sure erythema induratum was discussed also, and at the present time the use of some of the newer antituberculosis drugs has been reported to be fairly effective, but that certainly has not been our experience. I think that the treatment is not a specific one; the lesion having been formed the treatment is against the pathology rather than against the etiology, and if a focus of tuberculosis can be found it should be eliminated, if possible, by treatment directed against it.

DR. PAUL A. O'LEARY, Rochester, Minn.: I agree with the idea that the diagnosis of ulcers of the lower leg on morphologic features alone is difficult. We know of 41 separate entities, and there are probably more, which produce ulcerations on the lower extremities, and we suggested the term nodular vasculitis because of the patients with ulcers on the legs which were clinically suggestive of erythema induratum but in whom we were unable to demonstrate evidence of tuberculosis in any form, past or present. So our purpose was to emphasize the fact that tuberculosis was not always the cause of lesions like those presented by this patient.

The important point in the diagnosis of ulcerations of the leg is the recognition of the corollary conditions, as the question of etiology is seldom established by the character of the ulcer. It is necessary to look for other background explanations as the cause of the great majority of these lesions on the lower extremities.

DR. H. MONTGOMERY, Rochester, Minn.: I agree with Dr. Michelson that the histologic picture of erythema induratum is not necessarily diagnostic. In fact, in the series of cases that Dr. Barker, Dr. O'Leary, and I reported in the Clinic of nodular vasculitis the histologic picture was diagnostic in only 60% of the cases of erythema induratum. The patient presented had a biopsy performed elsewhere, in which the diagnosis of erythema induratum was made and tubercle bacilli were demonstrated in the section. The patient has a very strong tuberculin reaction, and the frozen sections of the biopsy specimen taken here show a thrombophlebitis with several epithelioid cells. There is no question that it is vasculitis. The clinical picture is rather unusual for erythema induratum, as is the clinical course of the disease to date.

DR. F. T. BECKER, Duluth: Erythema induratum has ceased to be a therapeutic problem in our area, as we are fortunate in having beds available in the local tuberculosis sanatorium. The patients are given tuberculosis therapy for six to eight weeks, and the lesions usually heal.

DR. GEORGE BROCK, Winnipeg, Man., Canada: The history can be all-important in making a diagnosis of erythema induratum. A 19-year-old married woman consulted me regarding the recent eruption of indurated nodules on her legs. Her father had died of tuberculosis 12

years ago, and two sisters had also died of tuberculosis since that time. She was being checked regularly at the central tuberculosis clinic. No foci of tuberculosis could be demonstrated until the nodules appeared on the legs, after which the tuberculin test became positive 3 +. In 1941, her tuberculin test was 1 +.

Chronic Discoid Lupus Erythematosus.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.: These two cases were presented to permit our calling to your attention the value of quinacrine (Atabrine) hydrochloride in the treatment of lupus erythematosus. In October, 1951, Francis Page reported on the use of quinacrine hydrochloride in this disease (Page, F.: Treatment of Lupus Erythematosus with Mepacrine, *Lancet* **2**:755-758 [Oct. 27] 1951). I started using it in January, 1952, and have treated 30 patients thus far, with exceptionally good therapeutic results. Dr. Kierland, who had a large experience with quinacrine in the South Pacific, is more conservative in its use than I am, because of the many complications he encountered there. Many of us saw the great variety of skin eruptions which developed in the soldiers overseas, so that these serious reactions, including the blood dyscrasias, must be kept in mind if quinacrine is to be given to patients with lupus erythematosus.

I have had 3 patients with dissemination (chronic discoid with dissemination and subacute dissemination) who have fared unfavorably because of a rapid development of new skin lesions, which we now believe were not lupus erythematosus but rather a dermatitis medicamentosa, as these lesions cleared when the quinacrine treatment was stopped. Quinacrine cannot be used indiscriminately in all patients with lupus erythematosus, and it should be limited, I believe, until our experience increases, to the frank chronic discoid types.

Several patients who have returned for this treatment have had lupus erythematosus for 20 or more years and have received all the recommended forms of treatment, including periods of complete rest in bed for as long as three months, without deriving material benefit. After the institution of quinacrine therapy, however, they have all been remarkably improved.

Dr. Page suggested giving 100 mg. three times a day for a week, then 100 mg. twice a day for a week, then continuing with 100 mg. once a day. I have given some patients three tablets a day of 100 mg. each for several months. Their skin becomes yellow, but they do not object to that very greatly, as the color fades out when the quinacrine treatment is stopped. It is well to check the white blood cell count from time to time, and the minute there is evidence of dissemination or the appearance of new skin lesions, the drug should be discontinued.

It has been remarkable the way in which the chronic thick heavy plaques of lupus erythematosus have faded out in a period of 8 or 10 weeks, and I am continuing to give these patients one tablet a day or one tablet every other day, even though the lesions have involuted. Further experience and time will be necessary to determine just how permanent is the improvement these patients show.

DR. GEORGE BROCK, Winnipeg, Man., Canada: I was very happy to hear the remarks of Dr. O'Leary on the use of quinacrine. I have four patients with chronic discoid and two with subacute disseminate lupus erythematosus who are taking the drug. They were at first given 100 mg. three times a day until their skin became yellow, then the dose was reduced to 100 mg. twice a day. Two of the patients with chronic discoid have had the disease since the 1930's. One of them had gold therapy in the 1930's. To date they have all improved to such a degree that they are very pleased.

Both patients with subacute disseminate conditions have improved steadily. One of these was very ill in 1935. She suffered a mild relapse in January, 1952. All the patients have taken quinacrine for three months.

DR. PAUL A. O'LEARY, Rochester, Minn.: Dr. Page reported one case of subacute lupus erythematosus in which the patient did very well, but from our experience to date, I believe that it is advisable to proceed with great caution in treating such patients with quinacrine.

DR. L. A. BRUNSTING, Rochester, Minn.: Any procedure which offers promise in the control of chronic discoid lupus erythematosus is certainly welcome. As Dr. O'Leary has stated, our

experience with the use of quinacrine confirms the favorable effects of the drug as reported by Page from Betley's service in London (*Lancet* **2**:755 [Oct. 27] 1951). The second patient is a case in point. For almost 15 years, this woman has been subjected to constant treatment according to the vogue of the moment. While her disease was relatively mild for the first 10 years, the process has increased subsequently so that the lesions have become numerous and of profound intensity, with deep scarring, and all previous treatment, including the use of gold salts, vitamin E, and cortisone have brought about only temporary improvement. After three months of quinacrine therapy, 100 to 200 mg. a day, there have been no new lesions and the old ones have resolved almost completely. In our experience, untoward reactions from quinacrine in this group of patients have occurred almost entirely in those who have shown systemic repercussions of the disease, that is, leucopenia, elevated sedimentation rate, fever, arthralgia, and a questionable Hargraves' reaction in the blood.

DR. JOHN D. KRAFCHUK, Minneapolis: In the face of the present optimism concerning this new form of therapy, it might be worth mentioning that during a recent visit to Dr. Hellier's Clinic at the University of Leeds in England (service of Professor Ingram) four consecutive cases of chronic discoid lupus erythematosus were seen in which therapy with quinacrine hydrochloride (Mepacrine [Atabrine]) for up to three months' time had resulted in no apparent improvement. It may also be added that a recent report in the *British Medical Journal* describes the rather dramatic alleviation of symptoms in rheumatoid arthritis treated in this manner. During a recent visit to the Hôpital St. Louis in Paris, it was indicated that favorable results have also been observed with this drug in cases of Senear-Usher pemphigus, although in one case presented, in which the patient had intensely yellow skin, persistence of activity was shown in some of the lesions even after three months of therapy.

Mycosis Fungoides of Forty-Seven Years' Duration.
Mycosis Fungoides—Reticulum Cell Sarcoma.
Lymphoma.
Kaposi's Multiple Idiopathic Hemorrhagic Sarcoma.
Case for Diagnosis: Bullous Eruption.
Dermatitis Herpetiformis.
Pemphigus Vulgaris.
Dermatitis Herpetiformis.
Dermatitis Herpetiformis (in Father and Son).
Localized Myxedema.
Recalcitrant Pustular Eruption vs. Pustular Psoriasis.
Ichthyosiform Erythroderma.
Bullous Urticaria Pigmentosa.
Facial Granuloma with Eosinophilia.
Chronic Superficial Discoid Lupus Erythematosus of the Face.

News and Comment

ANNOUNCEMENTS

Course in Occupational Skin Problems.—A course of instruction in Occupational Skin Problems will be presented jointly by the Division of Occupational Health of the Public Health Service, the Department of Dermatology and Syphilology of the University of Cincinnati, and the Department of Preventive Medicine and Industrial Health, during the week of Oct. 12-16, 1953. The object of the course is to give physicians a greater understanding of cutaneous problems of occupational origin.

The program will be divided into three daily sessions, consisting of morning lectures and clinical demonstrations, afternoon field instruction in industrial plants, and evening panel discussions. The didactic presentations will include a review of the anatomy, physiology, and chemistry of the skin. Consideration will be given to the etiology, clinical appearance, diagnosis, and treatment of occupational dermatoses. This will be supplemented by discussions of specific measures of prevention and control. The evening sessions, in panel form, have been designed to present current information on the subjects of cutaneous cancer, cutaneous allergy, and medicolegal problems.

Dr. Louis Schwartz, former Chief, Industrial Dermatoses Section, U. S. Public Health Service, will be the guest speaker at the one dinner meeting. He will describe his personal experiences with these problems during the past 25 years.

Physicians interested in attending the course should write for application blank to Secretary, Institute of Industrial Health, Kettering Laboratory, Eden and Bethesda Aves., Cincinnati 19. A registration fee will be charged, and early application is advised since attendance will be limited.

Directory of Dermatologic Societies *

INTERNATIONAL

International Congress of Dermatology and Syphilology

Guido Meischer, Chairman, International Committee, Zurich, Switzerland.
Sven Hellerström, Secretary, International Committee, Stockholm, Sweden.
Place: Stockholm. Time: 1957.

Pan American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

Joseph J. Eller, President, 745 Fifth Ave., New York 22.
John G. Downing, Secretary, 520 Commonwealth Ave., Boston.
Place: Floating Medical Congress for 1954, including a three-day medical meeting in Caracas, Venezuela, in addition to visiting other Caribbean countries which were not visited in 1953. Time: January 11-14, 1954, Caracas, Venezuela.

FOREIGN

The British Association of Dermatology

J. E. M. Wigley, President, 132, Harley St., London, W.1.
G. B. Dowling, Secretary, 24, Wimpole St., London, W.1.

British Association of Dermatology and Syphilology (New South Wales Branch)

W. K. Myers, President, 135 Macquarie St., Sydney, Australia.
A. G. Finley, Secretary, 335 Macquarie St., Sydney, Australia.
Place: Royal North Shore Hospital, St. Vincent's Hospital, Sydney Hospital, Lewisham Hospital, Royal Prince Alfred Hospital, Royal Alexandra Hospital for Children, and Royal Newcastle Hospital. Time: 4:00 p.m., on Fridays, approximately every two months.

Canadian Dermatological Association

G. Brock, President, 413 Medical Arts Bldg., Winnipeg, Man.
A. Birt, Secretary, 429 Medical Arts Bldg., Winnipeg, Man.
Place: Winnipeg. Time: 1953.

Dermatological Association of Australia

M. R. Healy, President, 110 Collins St., Melbourne.
R. F. A. Becke, Secretary, 139 Macquarie St., Sydney.
Place: Adelaide. Time: 1953.

German Society of Dermatology

Alfred Marchionini, Chairman, Dermatological Clinic, University of Munchen.
Otto Grütz, Secretary, Dermatological Clinic, University of Bonn.

Israeli Dermatological Society

A. Dostrovsky, Chairman, Hebrew University Hadassah Medical School, Jerusalem.
Felix Sagher, Secretary, Hebrew University Hadassah Medical School, Jerusalem.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

New Zealand Dermatological Society

R. F. Thomas, President, A. M. P. Buildings, Queen St., Auckland.
B. H. R. Hill, Secretary, Bowman's Bldg., Market St., Napier.

North British Dermatological Society

President: Senior dermatologist in city where meeting is held.
P. W. Hannay, Honorary Secretary, 22 Nile Grove, Edinburgh 10, Scotland.

Royal Academy of Medicine in Ireland, Section of Dermatology

M. Drummond, President, 22, Upper Fitzwilliam St., Dublin.
B. Solomons Jr., Secretary, 42, Fitzwilliam Sq., Dublin.
Place: Royal College of Physicians of Ireland. Time: Approximately every two months.

Royal Society of Medicine, Section of Dermatology

G. B. Dowling, President, 24, Wimpole St., London, W.1.
D. I. Williams and H. E. Vickers, Secretaries, 1, Wimpole St., London, W.1.
Place: Royal Society of Medicine, 1 Wimpole St., London, W.1. Time: 4:00 p.m., third Thursday of each month.

Sociedad Cubana de Dermatologica y Sifilografia

Roberto Quero Padilla, President, Manzana de Gomez No. 222, Havana, Cuba.
Guillermo Gonzalez Peris, Secretary.

Sociedad Mexicana de Dermatologia

Silvestre Rico, Chairman.
Fernando Latapi, Secretary, Zacatecas 220 6, México, D. F.
Place: National School of Medicine, México, D. F. Time: 9:00 p.m., first Thursday of each month.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

George M. Lewis, Chairman, 66 E. 66th St., New York 21.
J. Walter Wilson, Secretary, 3875 Wilshire Blvd., Los Angeles 5.
Place: New York. Time: June 21-25, 1953.

American Academy of Dermatology and Syphilology

Michael H. Ebert, President, 55 E. Washington St., Chicago 2.
John E. Rauschkolb, Secretary, 25 Prospect Ave., N.W., Cleveland 15.
Place: Palmer House, Chicago. Time: Dec. 5-10, 1953.

American Board of Dermatology and Syphilology

Anthony C. Cipollaro, President, 40 E. 61st St., New York 21.
George M. Lewis, Secretary, 66 E. 66th St., New York 21.

American Dermatological Association

Louis A. Brunsting, President, 102 Second Ave. S.W., Rochester, Minn.
J. Lamar Callaway, Secretary, Duke Hospital, Durham, N. C.
Place: The Greenbriar, White Sulphur Springs, W. Va. Time: April 14-17, 1954.

SOCIETY FOR INVESTIGATIVE DERMATOLOGY

Arthur C. Curtis, President, University Hospital, Ann Arbor, Mich.
Herman Beerman, Secretary, 255 S. 17th St., Philadelphia 3.
Place: San Francisco. Time: June 19, 20, 1954.

SECTIONAL

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

Marvin Winer, President, 333 Linwood Ave., Buffalo 9.
Frank A. Dolce, Secretary, 568 Delaware Ave., Buffalo 2.

NEW ENGLAND DERMATOLOGICAL SOCIETY

Mildred Ryan, President, 57 W. Elm St., Brockton, Mass.
Joseph Goodman, Secretary, 375 Commonwealth Ave., Boston.
Place: New Haven Hospital, New Haven, Conn., and Massachusetts General and Boston City hospitals (in alternation), Boston.

PACIFIC DERMATOLOGIC ASSOCIATION

Norman N. Epstein, President, 450 Sutter St., San Francisco.
Ervin Epstein, Secretary, 447 29th St., Oakland, Calif.
Place: Seattle, Wash., Olympic Hotel. Time: July, 1953.

PACIFIC NORTHWEST DERMATOLOGICAL SOCIETY

Sam E. Light, President, Medical Arts Bldg., Tacoma, Wash.
Leon F. Ray, Secretary, 628 Medical Dental Bldg., Portland 5, Ore.
Place: Place varies. Time: Third Thursday of May and October.

ROCKY MOUNTAIN DERMATOLOGIC SOCIETY

Gerald M. Frumess, President, 2200 E. 18th Ave., Denver.
Thomas W. Moffatt, Secretary, 822 Majestic Bldg., Denver.
Place: Selected prior to each meeting. Time: Selected prior to each meeting.

SOUTHEASTERN DERMATOLOGICAL ASSOCIATION

C. A. Andrews, Chairman, 706 Franklin St., Tampa, Fla.
Joseph Farrington, Secretary, 204 Laura St., Jacksonville, Fla.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY

D. Truett Gandy, President, 424 Medical Arts Building, Houston 2, Texas.
Ray O. Noojin, Secretary, 620 S. 20th St., Birmingham, Ala.

SOUTHWESTERN DERMATOLOGICAL SOCIETY

Samuel J. Jelso, President, Medical Arts Square, Albuquerque, N. M.
Robert H. Snapp, Secretary, 15 E. Monroe, Phoenix, Ariz.
Place: Various cities in Arizona, New Mexico, and Western Texas, in the fall; In conjunction with meeting of Rocky Mountain Dermatological Society, in the spring. Time: Fall and spring.

STATE

ALABAMA DERMATOLOGIC SOCIETY

William L. Poole, President, Woodward Building, Birmingham.
Irving D. London, Secretary, 746 Adams Ave., Montgomery.

Arkansas Dermatological Society

Davis W. Goldstein, Chairman, Cooper Clinic, Fort Smith.
Ray Fulmer, Secretary, 103 E. Seventh St., Little Rock.

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Rees B. Rees, Chairman, 380 Post St., San Francisco.
Frances M. Keddie, Secretary, 300 Homer Ave., Palo Alto.

Connecticut State Medical Society, Section on Dermatology

Joseph Becker, Chairman, 302 State St., New London.
Jack J. Albom, Secretary, 43 Trumbull St., New Haven.
Place: New Haven.

Florida Society of Dermatology and Syphilology

Lewis Capland, President, 350 Lincoln Road, Miami Beach 1.
Morris Waisman, Secretary, 1201 Citizens Bldg., Tampa 2.

Hawaii Dermatological Society

Harry L. Arnold Jr., Secretary, 881 S. Hotel St., Honolulu 53.

Indiana State Dermatological Society

Daniel Tweedal, President, 527 Sycamore St., Evansville.
Robert E. Jenkins, Secretary, 3311 N. Meridian, Indianapolis 8.

Louisiana Dermatologic Society

Lee McLean, Chairman, Pere Marquette Bldg., New Orleans.
F. C. Grieshaber, Secretary, Pere Marquette Bldg., New Orleans.
Place: Louisiana State Charity Hospital, New Orleans. Time: Third Sunday of each month

Massachusetts Medical Society, Section on Dermatology and Syphilology

Ethel M. Rockwood, President, 416 Marlboro St., Boston 15.
S. J. Messina, Secretary, 520 Commonwealth Ave., Boston 15.
Place: Hotel Statler, Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

George M. Lewis, President, 66 E. 66th St., New York 21.
Frank A. Dolce, Secretary, 468 Delaware Ave., Buffalo.

Michigan State Medical Society Section on Dermatology and Syphilology

J. R. Delaney, Chairman, 1020 David Whitney Bldg., Detroit 26.
C. J. Courville, Secretary, 1202 Maccabees Bldg., Detroit 2.

Minnesota Dermatological Society

Meriam G. Fredericks, President, 205 W. 2d St., Duluth.
Harold G. Ravits, Secretary, 546 Lowry Medical Arts Bldg., St. Paul.

New Jersey Dermatological Society

Frederick C. Licks, President, 64 Scotland Road, South Orange.
Seymour L. Hantling, Secretary, 115 S. Munn Ave., East Orange.

Oklahoma Dermatological Association

Phyllis Jones, President, 705 Medical Arts Bldg., Oklahoma City.
William G. McCreight, Secretary, 525 N. W. 11th St., Oklahoma City.
Place: Oklahoma City and Tulsa, alternately. Time: Semi-annually.

Rhode Island Dermatological Society

Carl D. Sawyer, President, 184 Waterman St., Providence.
Malcolm Winkler, Secretary, 199 Thayer St., Providence.

Texas Dermatological Society

Maurice G. Barnes, President, 3110 Austin St., Waco.
Thomas L. Shields, Secretary, 1216 Pennsylvania Ave., Fort Worth.
Place: Rotating. Time: Spring, coincident with Texas State Medical Association; fall, October.

LOCAL

Baltimore-Washington Dermatological Society

James Q. Gant, Jr., Chairman, 1726 M St., N.W., Washington, D. C.
Jack L. Derzavis, Secretary, 1835 Eye St., N.W., Washington, D. C.
Place: Baltimore and Washington. Time: Third Thursday of each month, in alternate cities, October to May.

Bronx Dermatological Society

Rudolf L. Baer, President, 962 Park Ave., New York.
Henry Silver, Secretary, 290 W. End Ave., New York.
Place: Academy of Medicine. Time: Third Thursday of every month, October to May.

Brooklyn Dermatological Society

Samuel I. Greenberg, President, 277 Eastern Parkway.
Harry L. Feigenbaum, Secretary, 352 77th St.
Place: Brooklyn Hospital Clinic, Ashland Place and DeKalb Ave. Time: Third Monday of each month, October to May.

Buffalo-Rochester Dermatological Society

Marvin Winer, President, 333 Linwood Ave., Buffalo.
Frank A. Dolce, Secretary, 468 Delaware Ave., Buffalo.
Place: Edward J. Meyer Memorial Hospital, Buffalo, and Strong Memorial Hospital, Rochester. Time: Second Tuesday of every month, October to May, inclusive.

Central New York Dermatological Society

Clarence J. Gabel, President, State Tower Bldg., Syracuse.
Julius Voehl, Secretary, 713 E. Genesee St., Syracuse.

Chicago Dermatological Society

Samuel J. Zakon, President, 185 N. Wabash Ave.
Irene Neuhauser, Secretary, 7 W. Madison, St.
Place: Chicago. Time: Third Wednesday of each month except June, July, August, and September.

Cincinnati Dermatological Society

Alfred L. Weinger, President, Union Central Bldg., Cincinnati.
Raymond R. Suskind, Secretary, Kettering Laboratory, University of Cincinnati, Cincinnati.
Place: Cincinnati General Hospital. Time: 8:00 p. m., first Wednesday of each month, October to May.

Cleveland Dermatological Society

Irving L. Schonberg, President, 1021 Euclid Ave. (15).
John R. Haserick, Secretary, Cleveland Clinic (6).

Dallas Dermatological Society

Bedford Shelmire, President, 1410 Medical Arts Bldg.
D. Shelton Blair, Secretary, 304 Medical Arts Bldg.
Place: Medical Arts Bldg. Time: Third Wednesday of each month.

Detroit Dermatological Society

Henry A. Brunsting, President, 2001 Collingwood Ave., Toledo, Ohio.
Charles J. Courville, Secretary, 1202 Maccabees Bldg. (2).

Kansas City Dermatological Society

Thomas B. Hall, President, 902 Professional Bldg., Kansas City 6, Mo.
Bernard H. Winston, Secretary, 324 Professional Bldg., Kansas City 6, Mo.
Place: University of Kansas Medical Center, Kansas City, Kan. Time: 10:00 a. m., second Sunday of each month, from October through June.

Long Island Dermatological Society

Charles S. Miller, President, Corona, N. Y.
Conrad Stritzler, Secretary, 90-26 148th St., Jamaica 2, N. Y.
Place: Queens General Hospital, Jamaica, N. Y. Time: Second Tuesday of each month, 8:00 p. m.

Los Angeles Dermatological Society

Walter Schwartz, President, 696 E. Colorado Blvd., Pasadena, Calif.
J. Walter Wilson, Secretary, 3875 Wilshire Blvd., Los Angeles.
Place: Good Hope Clinical Association. Time: Second Tuesday of each month, October to May.

Manhattan Dermatologic Society

Samuel Peck, President, 33 E. 70th St. (21).
George M. Lewis, Secretary, 66 E. 66th St. (21).
Place: Each member's office, in rotation. Time: 8:00 p. m., second Tuesday of each month.

Metropolitan Dermatological Society

Joseph C. Amersbach, President, 105 E. 53rd St., New York.
Valentine C. Baker, Secretary, 619 W. 140th St., New York.
Place: Offices of members. Time: Third Monday of each month, October to May.

Metropolitan Dermatological Society of Chicago

T. Benedek, President, 25 E. Washington St., Chicago 2.
Harold W. Thatcher, Secretary, 6 E. Garfield Blvd., Chicago 15.
Place: Chicago, alternating in the Services of the Fellows. Time: Second Wednesday, 10:00 a. m., from October to May.

Metropolitan Dermatological Society of Los Angeles

Stanton B. May, President, 119 N. Central Ave., Glendale, Calif.
Irving A. Lewe, Secretary, 3319 W. Beverly Blvd., Montebello, Calif.
Time: Fourth Tuesday of each month, October through May.

Milwaukee Dermatologic Society

M. J. Reuter, President, 324 E. Wisconsin Ave.
Donald M. Ruch, Secretary, 208 E. Wisconsin Ave.

Montreal Dermatological Society

Frederick Kalz, President, 1414 Drummond St.
B. P. Heller, Secretary, 1538 Sherbrooke St., W.
Place: Royal Victoria Hospital, Notre Dame Hospital, Montreal General Hospital, and other hospitals. Time: October, February, and April.

New York Academy of Medicine, Section of Dermatology and Syphilis

Anthony C. Cipollaro, Chairman, 40 E. 61st St. (21).
J. Lowery Miller, Secretary, 371 Park Ave.
Place: New York Academy of Medicine, 2 E. 103rd St. Time: First Tuesday of each month.

New York Dermatological Society

Anthony C. Cipollaro, Chairman, 40 E. 61st St. (21).
Maurice J. Costello, Secretary, 140 E. 54th St.
Place: New York. Time: Fourth Tuesday of each month.

Omaha Dermatological Society

Olin J. Cameron, President, 1520 Medical Arts Bldg.
George F. Pinne, Secretary, 453 Aquila Ct.

Philadelphia Dermatological Society

Bertram Shaffer, President, 1825 Pine St (3).
Lewis M. Johnson, Secretary, 203 N. Lime St., Lancaster, Pa.
Place: Philadelphia hospitals. Time: Third Friday of each month except June, July, and August.

Pittsburgh Dermatological Society

Samuel R. Perrin, President, 119 S. Highland Ave. (6).
William B. Guy, Secretary, 7026 Jenkins Arcade.
Place: Falk Clinic, 3601 Fifth Ave. Time: Third Thursday of each month.

San Francisco Dermatological Society

Edward A. Levin, President, 450 Sutter St.
Max E. Krause, Secretary, 400 29th St., Oakland, Calif.

St. Louis Dermatological Society

Joseph Grindon Jr., President, 539 N. Grand Ave. (3).
Morris Moore, Secretary, 3427 Washington Blvd.
Place: Barnard Free Skin and Cancer Hospital. Time: 8:00 p. m., third Monday of each month, October to May.

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Archives of Otolaryngology, March, 1947: 294-297

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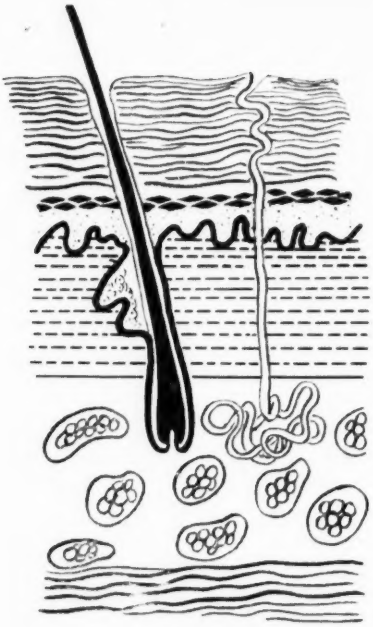

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468 Dewitt St., Buffalo 13, N. Y.